scientific reports

nature research

# Editorial Board Highlights

**Interviews**

Read exclusive interviews with some of our board members and learn about their research and their experience as a *Scientific Reports* board member.

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## Dr Carlo Cannistraci

*Dr Carlo Cannistraci is a Theoretical Engineer and Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

I am a Theoretical Engineer; my research interests include subjects at the interface between physics of complex systems, complex networks and machine intelligence, with particular interest in brain/bio-inspired computing for Big Data analysis, and applications in precision biomedicine and neuroscience.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

Mapping complex networks to their latent geometric spaces helps to investigate, understand and predict the structure and function of complex systems. My biggest challenge and greatest achievement was to recently propose a class of intelligent machines for efficient embedding of large real networks to the hyperbolic space, with future impact on big-network-data analysis in biology, medicine and social science. This work was proposed in the article: Machine learning meets complex networks via coalescent embedding in the hyperbolic space, A Muscoloni, JM Thomas, S Ciucci, G Bianconi, CV Cannistraci. Nature Communications 8 (1), 1, 2017.

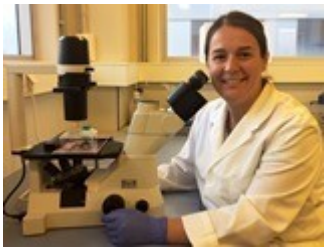
### 3. Why did you decide to become a board member?

I love to support other colleagues to improve their studies and to achieve high standards in their publications. This is the spirit of the review process: to offer feedback that improves science and its dissemination with a clear benefit for all of the scientific community.

### 4. What do you like most about being a board member for *Scientific Reports*?

Being an Editor for *Scientific Reports* for me is something more than being a normal Editor. The spirit of *Scientific Reports* is the spirit of 'freedom and equal opportunity' in science. I like the fact that *Scientific Reports* accept articles according to the only requirement that they should be technically correct. This ensures that the article selection is not biased by the opinion of a 'group of experts' that, in my opinion, can be also risky, because very innovative ideas that are against the mainstream in science might be rejected. I feel that being an editor for *Scientific Reports* allows me to sponsor the freedom to publish new scientific ideas which are technically correct but might not be recognised by a conservative establishment of experts.

## Dr Joana Maria Ramis



*Dr Joana Maria Ramis is a Miguel Servet Researcher at the Balearic Islands Health Research Institute (IdISBa), as well as Adjunct Lecturer at the University of the Balearic Islands, Spain.*

### 1. What is your current research focused on?

My research is focused on the development of new therapies and biomaterials for restorative and regenerative medicine and its translation to clinical practice. My newest research line focus on the approach to cell-free regenerative medicine through the use of extracellular vesicles derived from different cells types.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

My biggest challenge and greatest achievement has been, and keeps being, reconciling family life and my research career.

### 3. Why did you decide to become a board member?

I considered the offer to become a board member as a great opportunity to deepen in the knowledge of the review process and to be an active part of it. Publication of our results is an important part of our work as researchers, and before becoming a board member for *Scientific Reports*, I have only acted as author or as reviewer, thus, to act as editorial board member was a role I was interested in exploring.

**4. What do you like most about being a board member for *Scientific Reports*?**

Being a board member for *Scientific Reports* allows me to be updated in the ongoing research in my areas of expertise and to really deepen in the technical aspects of the manuscripts I handle. On top of that, the most positive aspect of being a board member is how much I learn from the interaction with the reviewers and the authors and how manuscripts improve from it.

**5. You are leading one of our Guest Edited Collections. What interested you about becoming a Guest Editor? What is your Collection focused on?**

Yes, I am leading the Special Collection entitled "Extracellular vesicles in cell biology and medicine". The collection is focused on extracellular vesicles (EV), cell-derived membranous structures known as intercellular communicators exerting their function by exchanging their cargo. EV research is a burgeoning field with a high number of researchers from different disciplines working in this field. This Special Collection intents to deliver an up-to-date overview on some of the current developments in the field.
To increase my interaction with other researchers of the field is what most interested me about becoming a Guest Editor for the Collection.

**6. Which is your favourite *Scientific Reports* paper?**

It is really difficult to select one single paper! I will list you some:

Cells release subpopulations of exosomes with distinct molecular and biological properties.
Willms, E.; Johansson, H. J.; Mäger, I.; Lee, Y.; Blomberg, K. E. M.; Sadik, M.; Alaarg, A.; Smith, C. I. E.; Lehtiö, J.; El Andaloussi, S.; Wood, M. J. A.; Vader, P.

Size-Exclusion Chromatography-based isolation minimally alters Extracellular Vesicles' characteristics compared to precipitating agents.
Gámez-Valero, A.; Monguió-Tortajada, M.; Carreras-Planella, L.; Franquesa, M. la; Beyer, K.; Borràs, F. E.

Labeling Extracellular Vesicles for Nanoscale Flow Cytometry.
Morales-Kastresana, A.; Telford, B.; Musich, T. A.; McKinnon, K.; Clayborne, C.; Braig, Z.;

Rosner, A.; Demberg, T.; Watson, D. C.; Karpova, T. S.; Freeman, G. J.; DeKruyff, R. H.; Pavlakis, G. N.; Terabe, M.; Robert-Guroff, M.; Berzofsky, J. A.; Jones, J. C.

Bone marrow stromal/stem cell-derived extracellular vesicles regulate osteoblast activity and differentiation *in vitro* and promote bone regeneration *in vivo*.
Qin, Y.; Wang, L.; Gao, Z.; Chen, G.; Zhang, C.

Exosomes derived from human adipose mensenchymal stem cells accelerates cutaneous wound healing via optimizing the characteristics of fibroblasts.
Hu, L.; Wang, J.; Zhou, X.; Xiong, Z.; Zhao, J.; Yu, R.; Huang, F.; Zhang, H.; Chen, L.

## Professor Xiaochun Li

*Professor Xiaochun Li is the Raytheon Endowed Chair in Manufacturing Engineering at the Departments of Mechanical and Aerospace Engineering & Materials Science and Engineering at UCLA, USA. He is also a Guest Editor for the Nanotechnology enabled metallurgy Collection, which is currently welcoming submissions.*

### 1. What has been your biggest challenge and your greatest achievement in your career so far?

The biggest challenge has been to bridge science and manufacturing for long term impact. The greatest achievement in my career so far is the discovery of the nano-particle self-dispersion and stabilisation mechanism in molten metals, which establishes a scientific foundation for nanotechnology enabled metallurgy.

### 2. Why did you decide to become a board member?

Being a board member is a good opportunity to provide a valuable service to the technical community.

### 3. What do you like most about being a board member for *Scientific Reports*?

My greatest pleasure is to help make the review process better, while having the opportunity to Guest Edit a special Collection.

### 4. You are leading one of our Guest Edited Collections. What interested you about becoming a Guest Editor? What is your Collection focused on?

I really like the opportunity to promote an important emerging field, Nanotechnology enabled metallurgy.

### 5. Which is your favourite *Scientific Reports* paper?

Core-shell nanoparticle arrays double the strength of steel

J.-B. Seol et al.

## Professor Luciano Bosso

*Professor Luciano Bosso is an Assistant Professor of Ecology at the University of Naples Federico II.*

### 1. What is your current research focused on?

I am an ecologist expert in ecological modelling and GIS analysis. My main research interests include conservation biology, global change ecology, biogeography and invasion ecology and the application of species distribution models, niche analysis, risk mapping, conservation gap analysis, landscape ecology, spatial analysis, species connectivity and corridor network simulation.

### 2. What have been your biggest challenge and your greatest achievement in your career so far?

My biggest challenge is to make scientific research more accessible and comprehensible to a wider non-scientific audience. I am particularly devoted to increasing the ecological knowledge of non-experts. Several of my studies have informed policy makers about best management strategies of protected areas in Italy and Europe, and I consider this use of my research as my greatest achievement.

### 3. Why is *Scientific Reports* one of your favourite journals?

*Scientific Reports* is a multidisciplinary journal that publishes scientifically valid primary research from all areas of the natural sciences and beyond. I have always admired the quality and rigour of the scientific studies published in this prestigious journal.

### 4. Why did you decide to become a board member?

Considering the crucial role that editors have in scientific communication, I was looking for an opportunity where I can apply and especially improve/broaden my editorial skills as well as find professional and personal satisfaction both as an editor and a scientist. I am very grateful to *Scientific Reports* for this exciting opportunity.

**5. What do you like most about being a board member for *Scientific Reports*?**
I am particularly satisfied by the opportunity to enrich my background, collaborate in an international context, and contribute to the journal's high-quality publication standards.

**6. Which is your favourite *Scientific Reports* paper?**
It is really difficult to select a single paper! I was really impressed by these recent publications:

Integrating experimental and distribution data to predict future species patterns.
Kotta et al. (2019).

Risk of biodiversity collapse under climate change in the Afro-Arabian region.
Soultan et al. (2019).

Climate change-driven range losses among bumblebee species are poised to accelerate.
Sirois-Delisle and Kerr (2019).

Modeling the distributions of tegu lizards in native and potential invasive ranges.
Jarnevich et al. (2018).

Assessment of the effect of climate changes in the Late Pleistocene and Holocene on niche conservatism of an arvicolid specialist.
Castellanos-Frías et al. (2018).

Can Niche Modeling and Geometric Morphometrics Document Competitive Exclusion in a Pair of Subterranean Rodents (Genus Ctenomys) with Tiny Parapatric Distributions?
Kubiak et al. (2017).

# Dr Ryoung Shin

*Dr. Ryoung Shin is a Unit Leader at RIKEN Center for Sustainable Resource Science.*

## 1. What is your current research focused on?

Potassium is one of major nutrients for plant growth, and lack of it in the soil environments has led to the increased use of fertilizers. However, such increased fertilizer usage does not necessarily result in a comparable production increase, and excess fertilizer run-off creates soil pollution. To address these issues, we elucidate the components of plant potassium sensing and deficiency signaling in plants using various approaches. In parallel, we are also using a marine red macroalgae *Pyropia yezoensis* in order to understand the mechanisms that enable seaweeds to survive in high salt conditions and to compare these mechanisms with those of the land plants in terms of $Na^+/K^+$ homeostasis. In addition, we identify and characterize chemicals which affect cesium and heavy metals uptake in plants to establish new methods of phytoremediation.

## 2. What has been your biggest challenge and your greatest achievement in your career so far?

My biggest challenge was starting the radiocesium phytoremediation research after the accident of Fukushima nuclear power plants following the big earthquake in Japan. It was a very challenging project (see here and here); and we are still actively working on this. One of my greatest achievements was that I have found and proven for the first time that Reactive Oxygen Species (ROS) is a key signal molecule of potassium-deficient signal transduction in plant roots.

## 3. Why did you decide to become a Board Member?

When I got the offer of being a Board Member, I recalled the time when we published two papers in *Scientific Reports*. It was an interesting and unique experience. *Scientific Reports* publishes articles from a variety of scientific backgrounds, including interdisciplinary research. Additionally, the editorial criteria for decision are different from other journals. I wanted to know more about this, and to be involved in *Scientific Reports* as a Board Member.

## 4. What do you like most about being a Board Member for *Scientific Reports*?

When I review the manuscript as a reviewer or handle the manuscripts as an editor, the manuscripts are usually from the specialised fields. At *Scientific Reports* I have really

enjoyed reading the interdisciplinary manuscripts. These are not easy because I should know many different fields to handle these manuscripts, but handling these papers gives me opportunity to learn about the various aspects and I can then see and appreciate the different angles.

### 5. Which is your favourite *Scientific Reports* paper?

One of my favourite *Scientific Reports* paper is "The antifungal plant defensin AtPDF2.3 from Arabidopsis thaliana blocks potassium channels" by Virens et al. Previously we found the link between Jasmonic acid signalling, including PDF genes and potassium/cesium signalling. This particular paper provides much more detailed insights into the relationship between PDFs and potassium channels. I really enjoyed reading this article. Recently, I have also had a pleasure of reading and handling a later published article "Effects of green seaweed extract on Arabidopsis early development suggest roles for hormone signalling in plant response to algal fertilisers" by Ghaderiardakani et al. This one was well balanced between the practical and basic scientific approaches using seaweeds. Ideas are attractive and the logical flow through was clear.

## Dr. Alberto G. Fairén

Alberto G. Fairén is an Astrobiologist at the Centro de Astrobiología in Madrid, Spain, a Visiting Scientist at the Department of Astronomy, Cornell University, and Editorial Board Member for Scientific Reports.

### 1. What is your current research focused on?

My research is focused on helping to understand the nature of the early Martian environments using a variety of tools from different disciplines: geomorphology, sedimentology, paleohydrology, geochemistry, aqueous mineralogy, and environmental microbiology. My research interests in Martian science are broad, spanning from surface evolution and habitability, to robotic exploration and mission design and operation. My research activities include a combination of theoretical modeling, laboratory experiments, field work and spacecraft data analysis.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

The biggest challenge has been keeping focus while moving among institutions, countries and continents, during my postdoc years. As soon as I got my PhD in Spain, I moved to NASA Ames in California for my postdoc, and later I worked for the SETI Institute also in California, and Cornell University in New York. After 8 years in the US, I returned to my home country and joined Centro de Astrobiologia, where I have recently got tenure. The journey has been challenging, but it also had its rewards, because the interaction with a wide variety of colleagues with different expertise and backgrounds allowed me to significantly grow in my career, and to reach my greatest achievements in publications, grants and awards.

**3. Why did you decide to become a board member?**

One of the most important tasks for a scientist is communicating the results of your investigations to the community. We, as researchers, should help to disseminate the scientific outcomes of our work. These responsibilities are essential for authors and reviewers indeed, but also for editors contributing to achieve high standards in publication quality, ethics, and fairness.

**4. What do you like most about being a board member for *Scientific Reports*?**

Being a board member for *Scientific Reports* is a good opportunity to provide a valuable service to the Mars community, helping to improve the review process facilitating the interactions between authors and reviewers, while contributing to Scientific Reports's high-quality publication standards. In addition, the only requirement for the publication of a paper in *Scientific Reports* is that they must be "technically correct original contributions", and they don't need to have a subjective significance as perceived by the editors, which may very well be erroneous and most likely biased.

**5. Which is your favourite *Scientific Reports* paper?**

It is very difficult to single one paper out, but I was really impressed by "Perchlorates on Mars enhance the bacteriocidal effects of UV light", by Wadsworth and Cockell, because of its significant implications to our current search for life on Mars. In addition, I recently had the pleasure of handling "The fate of lipid biosignatures in a Mars-analogue sulfur stream", by Tan et al., "A record of igneous evolution in Elysium, a major martian volcanic

province", by Susko et al., and "Seasonal deposition and lifting of dust on Mars as observed by the Curiosity Rover", by Vicente-Retortillo et al., three very impressive papers dealing with different aspects of Mars exploration.

## Professor Xuyang Lu

*Professor Xuyang Lu is an Associate Professor at the Institute of Mountain Hazards and Environment at the Chinese Academy of Sciences. He is an Editorial Board Member for* Scientific Reports *and is currently Guest Editing a Collection on Mountain surface processes and regulation, which is currently welcoming submissions until the end of September 2019.*

### 1. What is your current research focused on?

My academic research interests focus on the biogeochemical cycle and its microbial mechanism in mountain ecosystems. My recent work focuses on the effect of litter and soil organic matter chemistry on soil N transformation and its microbial function molecular ecological networks by comparing the China (Tibetan Plateau) and U.S. (Rocky Mountains) alpine ecosystems.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

I think my biggest challenge is the collection of soil and plant samples from alpine ecosystems, especially in the Tibetan Plateau. The plateau is considered to be the third "pole" of the world with an average elevation of 4 km above sea level. The natural environment is extremely harsh which characterized by high altitude, strong solar radiation, low temperatures and thin air. In this extreme environment, human survival is a challenge in itself, not to mention taking samples. In present, the greatest achievement in my career was that I discovered the influence extent and pattern of litter chemical composition and diversity on soil C, N transformation, which the related researches have

been published in Scientific Reports, Soil Biology & Biochemistry, Biology and Fertility of Soils.

### 3. Why did you decide to become a board member?

The first motivation is to learn how to become a qualified editor the academic journals. I feel a sense of accomplishment when a paper could reach the high-quality publication standard for *Scientific Reports* through the process of peer review and feedback with the authors.

### 4. What do you like most about being a board member for *Scientific Reports*?

I particularly like the criteria for publication in *Scientific Reports*, assessing an original article on the basis that they are technically sound and scientifically valid rather than innovation and importance, which provides the opportunity for more research works to be published. In addition, the Guest Edited Collection "Mountain surface processes and regulation", which I served as Guest Editor, supplies a high-quality publication platform for interdisciplinary studies of mountain surface processes and their responses to climate change and human activities. I sincerely appreciate *Scientific Reports* for this exciting opportunity.

### 5. Which is your favourite *Scientific Reports* paper?

Here I list three of my favourite *Scientific Reports* papers:
"A transnational perspective of global and regional ecosystem service flows from and to mountain regions", by Schirpke et al. (Article number: 6678, 2019).
"Altitudinal, temporal and trophic partitioning of flower-visitors in Alpine communities", by Lefebvre et al. (Article number: 4706, 2018).
"Planting increases the abundance and structure complexity of soil core functional genes relevant to carbon and nitrogen cycling", by Wang et al. (Article number: 14345, 2015).

## Professor Matjaž Perc

*Matjaž Perc is a Professor of Physics at the University of Maribor, Slovenia and Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

Climate inaction, the overexploitation of natural resources, and a harrowing gap between rich and poor are some of the most pressing issues of our time. Since these problems can't even be fully understood, let alone solved, from a perspective of a single scientific discipline, the future prospects of our societies will be determined by interdisciplinary and cross disciplinary research that cuts across different domains of science. We are working hard to make physics, particularly methods of statistical physics, together with network and data science, a key piece of this puzzle. Social physics enables us to theoretically describe and understand collective social phenomena that are due to the interactions among individuals, groups, and governments. From the responsible use of antibiotics and vaccination, to the mitigation of social crisis and inequalities, we aim to develop better social systems and more efficient policies for a sustainable and better future by synergizing physics with the social sciences.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

One of my career goals has always been to stay at my home university, and ultimately to get a permanent position there. This has turned out to be the biggest challenge, as well as the greatest achievement of my career. Slovenia is a small country. Research funding is scarce, and vacant tenure track positions are basically nonexistent. A consistently impressive research output is needed, along with some luck and sponsorship from senior colleagues, to finally make it. For me it worked out great, but for many talented researchers in Slovenia this reality means being forced to go work abroad.

### 3. Why did you decide to become a board member?

Being a *Scientific Reports* board member is for me a way to give back to the research community, and to promote and support the research field in which I am active. *Scientific Reports* always stood for high quality, but also for freedom and opportunity, which together with the open access policy make it a perfect outlet for the most innovative research. Such research is often difficult to publish in journals that judge impact and novelty because it often challenges the mainstream in science.

### 4. What do you like most about being a board member for *Scientific Reports*?

The role puts you right in the center of research that is close to your heart. It feels a little bit like having reserved the finest seats in the theater of science, getting to learn about fascinating new discoveries before they are officially published. I also very much enjoy good cover letters, where authors usually explain the gist of their research in simpler terms, discussing its broader implications, and pondering about potential impact and directions for the future.

### 5. Which is your favourite *Scientific Reports* paper?

My favorite *Scientific Reports* paper remains to be the first paper I have handled after joining the editorial board, titled "Flavor network and the principles of food pairing" published in 2011. The paper generated a lot of attention at the time, both in the scientific community and in the media, and it stands precisely for the type of avant-garde research I was hoping Scientific Reports would encourage. In this particular case opening new avenues towards a systematic understanding of culinary practice across the world. From my own publications in *Scientific Reports* my favorite is "Self-organization of progress across the century of physics" published in 2013, for its collaboration with the American Physical Society and the resulting n-gram viewer for physics that is akin to Google's version for books.

## Professor Yu Xin Zhang

*Professor Yu Xin Zhang is a Professor at the College of Materials Science and Engineering, Chongqing University, China. He is also a* Scientific Reports *Editorial Board Member and a Guest Editor for the Nanomaterials for energy and environmental applications Collection.*

### 1. What is your current research focused on?

My current research is mainly focused on the self-assembly of nanostructures with various morphologies, involving $MnO_2$ and diatomite-based nanocomposites, and their applications in energy storage and environmental fields.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

In my career, the biggest challenge was teaching Chinese students Technical Writing using English, which is my second language, while striving in materials science and engineering in Chongqing University. Indeed, it is highly important that teachers keep an eye on the learning process and abilities of students. Fortunately, my advisor, Prof. Hua Chun Zeng gave me a strict supervision in National University of Singapore, molding me to be a well-trained researcher and independent lecturer. In addition to being the biggest challenge in my career, teaching this course is also my greatest achievement. More than 5000 students who have had a direct or indirect contact with this course through me, have been able to improve their writing ability and some of them have even published their first article, which is a great motivation and confidence booster in scientific research, and nudged them to embark on the path of scientific research. I take pride in this.

### 3. Why did you decide to become a board member?

Becoming a board member is not only an endorsement of oneself, but also a means of staying abreast of the latest developments in scientific research, and actively communicating with international counterparts. Being a board member avails me these opportunities.

### 4. What do you like most about being a board member for *Scientific Reports*?

*Scientific Reports* is an outstanding journal, which publishes high quality articles with enormous future development prospects. I enjoy being able to make profound suggestions for the development of the journal, accepting excellent articles, and being able to learn substantially, even while doing something I love, and this is possible for me as a board member for *Scientific reports*. I like the rate at which the journal is developing in all aspects, it gets better and better.

## Professor Z. Altounian

*Professor Z. Altounian is a Professor in the Physics Department at McGill University, Montreal, Canada and Editorial Board Member for* Scientific Reports.

**1. What is your current research focused on?**

My current research is mainly focused on studies of magnetic properties of materials.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

Challenges always occur if one enters a new field of study. My first challenge started in the winter of 1979 when I got interested in metallic glasses. This was also my greatest achievement as our group at McGill University became a world famous centre in this field. I still contribute to this field, but mainly through editorial/reviewing responsibilities for journals and conferences. My second, and more recent challenge occurred when I got involved in the studies of magnetic properties of hard magnetic materials. It is worth to mention that there was a very close relationship between my two challenges as we used the technique of rapid solidification, which is commonly used to prepare metallic glasses, to manufacture rare-earth based magnets. This also brought us to worldwide recognition in this particular field.

**3. Why did you decide to become a board member?**

One of the aspects that drew me to become an EBM was the problems that I had encountered while reviewing manuscripts. Mostly the poor quality of some of the reviewers which in many cases did not agree on the evaluation of the same submission. In those cases, I was asked to make the final decision. As an EBM, I hoped to improve the reviewing protocol.

**4. What do you like most about being a board member for *Scientific Reports*?**

Prior to becoming an EBM, I was a very active reviewer for a number of publications in the above-mentioned fields. When *Scientific Reports* invited me to join their editorial team, I accepted the offer as I had always enjoyed reviewing journal submissions.

**5. Which is your favourite *Scientific Reports paper*?**

My favorite paper is SR 7, 646 (2017), "The magnetic and crystal structure of MnxGa (1.15 ≤ x ≤ 1.8) Alloys". This was our first publication in *Scientific Reports* as well as the first introduction to this fascinating material. Even-though we have been studying magnetic materials for more than two decades, this publication finally put us on the world map in this field.

## Dr Lena Ciric

*Lena Ciric is Associate Professor in Environmental Engineering at the Department of Civil, Environmental and Geomatic Engineering of University College London, UK. She is also a* Scientific Reports *Editorial Board Member and a Guest Editor for the Microbes in the built environment Collection.*

### 1. What is your current research focused on?

I am an environmental microbiologist. The environment I study is the built environment. My group works on two themes. The first is how microbes behave in the built environment. We have been studying the microbial communities and the horizontal gene transfer of antibiotic resistance genes in slow sand filtration, a commonly used drinking water treatment process. The other theme we study is how we can use engineering solutions to reduce the numbers of harmful microbes in our environment. We have been manufacturing water and air filters with antimicrobial nanoparticles embedded in them which are capable of killing bacterial and viral pathogens.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

I would say being an academic is both the biggest challenge and the biggest achievement of my career. The job can be extremely challenging as there are huge demands on your time. There is frequent failure – rejected grant applications, experiments that don't work, papers that are difficult to publish. But these challenges are also what motivates me. The job of an academic is so varied. We have the freedom to pursue our research ideas, we get to write, we get to read, collaborate, travel, interact with young people through teaching and speak to the public about our work. All of these experiences are extremely rewarding.

### 3. Why did you decide to become a board member?

I am naturally nosey, so I was curious to see what research is going on out there. As an editorial member you have the opportunity to reach out to experts in the field to help you scrutinise manuscripts and help the authors improve their work.

### 4. What do you like most about being a board member for *Scientific Reports*?

*Scientific Reports* has a novel approach. Instead of looking for the next big thing, it is happy to publish any scientific work that is technically sound. This is extremely useful to the scientific community. It means that we have a less biased view of the research going on around the globe.

### 5. Which is your favourite *Scientific Reports* paper?

Patterns in the skin microbiota differ in children and teenagers between rural and urban environments

I am fascinated by how the microbes that live on and in our bodies shape us physically and, some studies say, psychologically. I think it's wonderful to know that our body as an ecosystem rather than just one organism.

## Professor Kah-Wee Ang

*Prof. Kah-Wee Ang is Associate Professor in the Department of Electrical and Computer Engineering at the National University of Singapore.*

### 1. What is your current research focused on?

I am an experimentalist and my current research focuses on the development of both electronic and photonic devices based on two-dimensional (2D) materials, which include field-effect transistor and integrated circuit, non-volatile memory, artificial intelligence synapse for neuro-inspired computing, as well as electro-optic modulator and photodetector for mid-infrared sensing applications.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

I started off my research career exploring the use of beneficial strain effect to modify the carrier transport properties in the conduction channel for enhancing the mobility and drive current performance of nanoscale field-effect transistors (FETs). Specifically, I pioneered a novel concept in employing lattice-mismatched stressor made of silicon-carbon (Si:C) alloy in the source and drain regions of metal-oxide-semiconductor FETs,

which was widely evaluated by major semiconductor foundries worldwide. The technology was eventually adopted in high volume manufacturing, which gave me a sense of satisfaction and achievement.

Since five years ago, I started investigating two-dimensional materials for electronic and photonic device applications. As a new comer to this emerging field, many technical challenges were encountered which spanned across material synthesis, device fabrication to large-scale circuit and system integration. Through conscientious efforts, several advancements have been made in addressing module and process integration issues on flexible substrates, which allow energy-efficient logic gates, memories and sensors to be realized. Going forward, we aim to demonstrate a transformative 3D monolithic system via van der Waals integration of new logic and memory devices built on atomic-scale 2D materials, which can deliver a remarkable improvement in computational energy efficiency over traditional system architecture.

**3. Why did you decide to become a board member?**

Today the research landscape is dynamically changing where new exciting fields are emerging rapidly. Being an editorial board member allows me to not just keep up with the latest progress made in my field, but also gives me the opportunity to keep abreast of the new development that takes place across multidisciplinary fields. Getting to know the experts often helps me in assigning appropriate reviewers to assess the submitted manuscripts, and make constructive recommendations to improve the quality.

**4. What do you like most about being a board member for *Scientific Reports*?**

*Scientific Reports*' approach in publishing technically sound work and let the wider scientific community determine the impact of the work is well received by like-minded researchers including myself. This allows board member to avoid making subjective decisions on rejecting manuscripts which are perceived with little immediate interests but may grow in importance over time.

## Dr Pedro Oliveira

*Dr Pedro Oliveira is a Senior Scientist at Mount Sinai School of Medicine, USA.*

**1. What is your current research focused on?**

My current interests are on identifying emerging challenges in the fast-evolving research field of epigenomics, and on better understanding the epigenetic regulation mechanisms affecting gene expression and cellular processes in Bacteria. On a broader perspective, I seek to elucidate key biological insights that can translate into more accurate disease diagnosis and more effective treatment for certain bacterial pathogens.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

My biggest challenge has been in embracing some of the downsides of a career in academia, such as frequent failure and rejection, and being able to transform such missteps and roadblocks into an opportunity for something new. My greatest achievement as a researcher has been in help propelling the field of bacterial epigenomics. Such field has been attracting increased attention for its exciting potential to transform our knowledge on gene regulation, virulence, and adaptation. As an example, we recently performed the first large-scale comprehensive epigenomic analysis in *Clostridioides difficile*, known to be one of the leading causes of nosocomial antibiotic-associated disease in the developed world. We found evidence for epigenetic regulation associated with sporulation (a key step in *C. difficile* disease transmission), cell length, biofilm formation, and host colonization. For more information, please check: Oliveira *et al*. Epigenomic characterization of *Clostridioides difficile* finds a conserved DNA methyltransferase that mediates sporulation and pathogenesis. *Nature Microbiology*.

**3. Why did you decide to become a board member?**

Essentially, it was a great opportunity to become an active part of the decision-making process, while simultaneously helping the authors to achieve a higher quality standard in their publications. I am very thankful to *Scientific Reports* for this opportunity.

**4. What do you like most about being a board member for *Scientific Reports*?**

I particularly enjoy contributing to a journal that seeks high quality standards in its publications, focusing primarily on research robustness and validity, and less on subjective

editorial decisions. In this sense, *Scientific Reports* makes a distinctive contribution when compared with other journals. Furthermore, being a Board Member has given me the opportunity to learn and keep myself up to date on the latest research in my areas of expertise, while simultaneously delving into the multiple aspects of the manuscripts I handle.

### 5. Which is your favourite *Scientific Reports* paper?

It's difficult to highlight one single paper. I particularly enjoyed reading a recent publication describing a portable epigenetic switch for bistable gene expression in bacteria based on the *opvAB* operon of *Salmonella enterica*.

## Dr Ciria C. Hernandez

*Dr. Ciria C. Hernandez is an Assistant Research Scientist at the Life Sciences Institute, University of Michigan, USA. She is an Editorial Board Member for* Scientific Reports *and currently Guest Editing a Collection on Channelopathies, which is welcoming submissions on a rolling basis.*

### 1. What is your current research focused on?

The focus of my research has always been to understand the fine regulation of ion channels in physiological and pathological states. Thus, I have been fully immersed in the study of the molecular determinants of the interaction of small peptides, G-protein coupled receptors (GPCRs) and both voltage and ligand gated ion channels, whether they are defective or not, by carrying mutations in their structure that prevents them from normal function. Most recently, I have been working on the elucidation of the structural determinants of the interaction of GPCRs that mediate a variety of physiological processes critical for energy homeostasis, and potassium channels known to be involved in a novel G protein independent signaling pathway in a brain region that controls hunger. We are tackling the idea of bias agonism as a therapeutic approach to overcome defective GPCR-channel coupling in conditions where the rheostats of energy homeostasis are defective.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

My biggest challenge and my greatest achievement merge at the same point. Be competitive and remain relevant in the face of the unstoppable and continuing flow of new technologies. While this is true for any electrophysiologist, as a woman, coming from a developing country, there is a bigger challenge considering the general perception that you have about making a career in science, and still being able to respond to the demands of academia. Scientifically perhaps the biggest challenge is to understand how to fit every discovery I make, however small and trivial it may seem, in the greater puzzle we are helping to complete. We merge these pieces when we write the discoveries we made in the scientific articles, when we guide the youngest, and when we collaborate with peers from different fields. This is at the essence of science and my career has fundamentally been learning how to "put the pieces together" ever since I started my career. Although I have managed to break many barriers and be in a privileged position, I have not stopped learning and growing scientifically, and honestly, I will never stop doing it. This is my greatest achievement as a scientist.

### 3. Why did you decide to become a board member?

Being part of the editorial board of *Scientific Reports* implies transforming and transferring knowledge beyond critical thinking. We have to be not only the best scientists, but the best communicators. Being a board member of *Scientific Reports* made me realize how to communicate the passion that we scientists have for discovering the smallest molecular interactions and chats between receptors, channels, proteins, and bring them to public light. My passive voice became a strong megaphone through the publications of all the authors who contribute to making the best science in the world. By realizing that through my contribution, I am shaping the science that is read and at the same time inspiring me to be the best scientific communicator.

### 4. What do you like most about being a board member for *Scientific Reports*?

Each manuscript submitted is a challenge of new knowledge and unexpected creativity. The diversity of topics within our area of expertise is tremendous. It shows the high quality of science that is translated from the bench and witnessing that is unmatched and novel in many ways. At the same time, we are the role models for the challenges imposed in the current era, where the disparity of world economies challenges science in the quest for new discoveries.

### 5. Which is your favourite *Scientific Reports* paper?

Without reservations I invite you to read part of my work published in 2017 describing the defects on GABAA receptor function caused by deleterious mutations in cases with catastrophic epileptic encephalopathies, and many other fascinating studies on the special Collection dedicated to Channelopathies.

## Professor Claudia RC Moreno

*Prof. Claudia RC Moreno is Head of Department at the School of Public Health, University of Sao Paulo, Brazil and is currently an Editorial Board Member for Scientific Reports.*

### 1. What is your current research focused on?

The process of urbanization, as well as the use of electricity and its technology, has changed the way of life of society. The possibility of extending the waking period through the use of electric light changed working, sleeping, eating and leisure hours.  I have been studying communities with and without access to electricity with the focus on lifestyle, working hours, sleep and eating behavior.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

The biggest challenge was to run a study in the Amazon forest, collecting data from rubber tappers and having to freeze saliva samples to send to Sao Paulo, many kilometers away. It is hard to say my greatest achievement, but there are two things that I would like to highlight, first, the success of my former PhD students, and second, my participation on a monograph at the IARC-WHO regarding night shift work and cancer.

### 3. Why did you decide to become a board member?

*Scientific Reports* is a quite interesting journal due to its policy to evaluate papers technically sound. Moreover, I think it is important to have board members from Latin America.

### 4. What do you like most about being a board member for *Scientific Reports?*

It is a very dynamic task, and help me to keep myself updated.

### 5. Which is your favourite *Scientific Reports* paper?

My favorite paper is from an international group of researchers with focus on sleep in a rural cohort study. Timing and quality of sleep in a rural Brazilian family-based cohort, the Baependi Heart Study

## Professor Jimin Zhao

*Professor Jimin Zhao currently works in the Institute of Physics at the Chinese Academy of Sciences (CAS), Beijing, and is an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

I currently work on ultrafast spectroscopy and ultrafast dynamics of correlated quantum materials.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

The biggest challenge in my career so far is to convince my colleagues outside of my specific area that what I have done is reliable. This is especially challenging when our manuscripts are being reviewed, whereby very simple questions and unreasonable doubts come in by renowned yet non-experts in the field. I have investigated the ultrafast dynamics in novel iron-based superconductors and Weyl semimetals, I have also achieved SSPM and all-optical switching in 2D materials. I am currently a full professor at IOP-CAS and I am also an OSA senior member.

### 3. Why did you decide to become a board member?

Being a board member will open a new venue that I can do service to the community. Optical spectroscopy of solids is not a big area, and I feel my colleagues may need me to objectively judge on works using sophisticated optical means to investigate condensed matter physics.

### 4. What do you like most about being a board member for *Scientific Reports*?

Handling works in slightly different areas is interesting. My own experience can make a decisive contribution, whereas I can also enlarge my horizon through the handling process.

### 5. Which is your favourite *Scientific Reports* paper?

There are many. I remember one very good theoretical paper called Anomalous isotope effect in iron-based superconductors. I should say another one is one of our works. Out of the 6 papers I have published in *Scientific Reports*, our work Coherent Generation of Photo-Thermo-Acoustic Wave from Graphene Sheets, *Scientific Reports* 5, 10582 (2015) is my most favorite one. This work is highlighted in Chinese magazine *Physics*. It is a phenomenon parallel to photoluminescence. After we publish, I got to know that Alexander Graham Bell also worked on this topic and had filed a patent, and he thought it was one of his greatest achievements. Dr. Bell was a great scientist, and knowing this is wonderful. Nonetheless, before us, there are no serious and solid experimental proofs that cleanly removed other very possible mechanisms. We have also achieved remote coherent control of acoustic sound.

## Professor Amy Peterson

*Professor Amy Peterson is Associate Professor of Plastics Engineering at the University of Massachusetts Lowell, USA and is an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

My current research is focused on multilayered polymer structures – these range from nanometer-scale polyelectrolyte multilayers for cell culture coatings, to packaging materials, to additively manufactured structures. As engineers, we use experimental and computational approaches to probe what happens at interfaces and surfaces in these systems, and use this knowledge to guide creation/selection of improved materials and processes.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

This past week has been the most intensely challenging of my career. It ended with shutting down our laboratory on Saturday, but the lead up to that final act included figuring out what critical experiments were needed for each group member, attempting to get them approved as access to labs became increasingly restricted by my university, trying to keep my group up to date on the status of their possible experimental work, and doing all of this in a dynamic situation via phone, email, and videoconference. I feel fortunate because we have substantial modelling efforts as well as experimental ones, so we'll be able to continue to make progress on our research. However, my group meets weekly in person for group as well as one-on-one meetings, and I am concerned about how we will all fare being isolated in our homes.

My proudest moments are when I see my students succeed, whether it's at graduate, a defense, an award, a paper, or a presentation.

**3. Why did you decide to become a board member?**

Being a board member gives me an opportunity to give back to my broader research community and learn at the same time.

**4. What do you like most about being a board member for *Scientific Reports*?**

The same reasons I became a board member.

**5. Which is your favourite *Scientific Reports* paper?**

Clogging transition of many-particle systems flowing through bottlenecks – I like how it makes connections between systems of large numbers of people, flocks of sheep, and colloidal suspensions.

## Dr Jagadeesh Bayry

*Dr. Jagadeesh Bayry is Director of Research at the Institut National de la Santé et de la Recherche Médicale, Centre de Recherche des Cordeliers, Paris, France and is an Editorial Board Member for* Scientific Reports.

**1. What is your current research focused on?**

Our current research is focused on the mechanisms by which regulatory T cells and circulating immunoglobulins maintain immune homeostasis and deciphering the host-pathogen interaction.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

Though we identify mechanisms of various biological processes in the experimental systems, translation of these results to humans is always challenging. For that matter, I am proud of many achievements of my team and myself that include:

- Demonstration that regulatory T cells in contrast to central dogma on them as universal immunosuppressor cells, induce activation of human basophils (Science Immunology 2018. doi: 10.1126/sciimmunol.aan0829)
- Demonstration that surface hydrophobin protein layer prevents immune recognition of airborne fungal spores (Nature 2009. doi: 10.1038/nature08264)
- Demonstration of molecular mechanisms by which therapeutic normal immunoglobulin G expands regulatory T cells (Blood 2013. doi: 10.1182/blood-2012-11-468264) and induces induction of IL-4 in human basophils (J Allergy Clin Immunology 2019. doi: 10.1016/j.jaci.2018.10.064)
- Identification and validation of small molecule antagonists to CCR4 that function as molecular adjuvants in vaccination by transiently inhibiting the migration of regulatory T cells (Proc Natl Acad Sci USA 2008. doi: 10.1073/pnas.0803453105)
- Activation signal-dependent regulation of human dendritic cell functions by B lymphocytes (Nature Communications 2014. doi: 10.1038/ncomms5092)

**3. Why did you decide to become a board member?**

For me, it is a service to scientific community. Though it demands my time, I feel that it is a highly privileged position. In addition, it gives visibility to myself, team and institute.

**4. What do you like most about being a board member for *Scientific Reports*?**

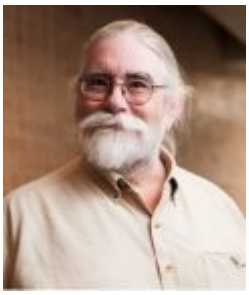
'Open Access' journals have been misinterpreted by some people as 'journals that can publish anything'. As an editorial board member, I ensure that low-quality studies are not published in Scientific Reports. One should not forget that currently there is huge demand

for external reviewers. Therefore, being a board member of journal, I can allow only original and technically sound articles for peer review.  It will reduce burden on the reviewers.

### 5. Which is your favourite *Scientific Reports* paper?

It is difficult to pick a single paper. I have many favourite *Scientific Reports* papers.

## Professor Timothy Geary



*Prof. Timothy Geary is a Professor in the Institute of Parasitology in the Faculty of Agricultural and Environmental Sciences at McGill and is an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

I do research in two areas: the pharmacology of antiparasitic drugs (including drug target identification, mechanisms of action and resistance, and development), and understanding the molecular language of the host-parasite interface, with an emphasis on nematodes. The primary focus of this work is the identification and characterization of parasite-derived proteins, metabolites and miRNAs that have immunomodulatory activity in the mammalian host, enabling the establishment of chronic infections.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

It's always hard to rank an event as #1 in these areas.  Certainly, a major challenge was transitioning from a 20-year career in the pharmaceutical industry to a 15-year career in academia at McGill and now also QUB. The switch was made possible by the Canada Research Chairs programme, which enabled me to get started at McGill, and by support from the Bill and Melinda Gates Foundation, which enabled me to use some of the technology I had developed in the industry to conduct an innovative drug discovery program with partners in Africa.  The greatest achievement may have been research that provided a plausible explanation for how the anthelmintic ivermectin removes larval stages of filariid nematodes (microfilariae) from hosts, a key action that makes the drug of value in filariasis control programmes. In another sense, my greatest achievement has

been to work with enormously talented colleagues around the world in fascinating areas of research.

### 3. Why did you decide to become a board member?

It is an honour to be asked to contribute to the success of one of the Nature family of journals, and I was flattered to be invited. I am on the editorial boards of a number of journals in parasitology, and am glad to serve in that capacity, but *Scientific Reports* addresses broader topics; I wanted to make sure that parasite-related manuscripts submitted here would be fairly and rigorously evaluated.

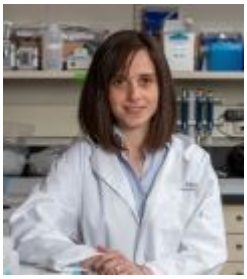
### 4. What do you like most about being a board member for *Scientific Reports*?

I enjoy the breadth of manuscripts sent to me to consider as board member. Also – and importantly – the staff assistance is exceptional and makes the tasks associated with securing reviews much easier. It is a pleasure to work with them.

### 5. Which is your favourite *Scientific Reports* paper?

This I cannot answer….there have been too many to rank. I am confident that they have all been valuable additions to the literature.

## Dr Leyla Soleymani



*Dr. Leyla Soleymani is a Professor and Canada Research Chair at McMaster University and an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

My current research is focused on creating new hierarchical materials and applying these to biosensors and antimicrobial surfaces.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

I guess my greatest achievements and greatest challenges are related. I have found it challenging to balance the needs of an industry relevant product with the required novelty

for successful scientific publication. Some of my proudest achievements have been on technology development activities that are in the process of being translated to knowledge users.

### 3. Why did you decide to become a board member?

I highly respect the peer-review process and I find it critically important for advancing science. Being an editorial board member at *Scientific Reports* allows me to take part in overseeing the peer review process and work in ensuring that a fair and transparent process is followed, to get the first scoop on new and exciting papers, and to contribute to the publication of high quality papers, not just as an author or a peer reviewer but also as an editorial board member.

### 4. What do you like most about being a board member for *Scientific Reports*?

I get to read new papers in more diverse areas that I would normally read, which gives me inspiration and insight.

### 5. Which is your favourite *Scientific Reports* paper?

It is tough to choose an all time favourite, but recently I came across this paper "Logistic growth of a surface contamination network and its role in disease spread" and found it eye-opening in the context of the COVID-19 pandemic.

## Dr Ruth Blasco

*Dr Ruth Blasco is Taphonomy researcher at Centro Nacional de Investigación sobre la Evolución Humana (CENIEH), Burgos, Spain and is an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

My current research explores human subsistence strategies during the Pleistocene using a taphonomic approach. I am trying to determine several aspects of human behaviour from the faunal record and contribute to evolutionary anthropology by developing several research sub-areas, such as butchery patterns and hominid–carnivore interactions.

**2. What has been your biggest challenge and your greatest achievement in your career so far?**

Documenting an intentional delayed consumption of some animal resources (specifically bone marrow from fallow deer metapodials) with implications that affect the subsistence systems of more than 300 thousand years ago.

Food storage is considered a "risk-reducing mechanism" designed to offset downturns in resource availability. The deliberate accumulation of some bones for later marrow consumption implies an anticipation of and concern for future needs. This fact marks a threshold for new modes of Palaeolithic adaptation because the foresight capacity surpasses the "here and now" as a means of subsistence. This study was published last year in Science Advances [Blasco, R., Rosell, J., Arilla, M. ,Margalida, A.,Villalba, D., Gopher, A., Barkai, R., Bone marrow storage and delayed consumption at Middle Pleistocene Qesem Cave, Israel (420 to 200 ka). Sci. Adv. 5, eaav9822 (2019)].

**3. Why did you decide to become a board member?**

I think that the peer-review process is a fundamental tool for generating quality scientific production. Participating in this process not only as an author or a reviewer but also as an editorial board member allows me to ensure that these processes are objective and transparent and that rigorous, novel and exciting studies are released. I consider it to be a highly privileged position as well as a way of serving the scientific community.

**4. What do you like most about being a board member for *Scientific Reports*?**

Beyond reading papers from very diverse areas that continuously broaden my knowledge and inspire my future work, being a board member for *Scientific Reports* has allowed me to lead and handle a special collection on "Quaternary Taphonomy" that involves trans- to pluri-disciplinary approaches, such as archaeology, palaeontology, geology, biology and ecology, with a wide array of methodologies. The number of researchers working on taphonomy is steadily increasing, and their contributing to high-ranked scientific journals is becoming a regular trend. This collection is gathering some of the most relevant current studies within this field in the attempt to become a reference source for further studies.

**5. Which is your favourite *Scientific Reports* paper?**

It is difficult to choose a specific paper, but I will highlight "Deep learning and taphonomy: high accuracy in the classification of cut marks made on fleshed and defleshed bones

using convolutional neural networks", which is a clear example of how the recent application of machine learning algorithms to the taphonomic discipline is achieving higher accuracy in the identification of bone surface modifications and the agents and/or processes that produce them.

## Dr. Feng Gao

*Dr. Feng Gao is a Professor in the Department of Physics, School of Science, at Tianjin University, Tianjin, China and an Editorial Board Member for* Scientific Reports.

### 1. What is your current research focused on?

I am engaged in bioinformatics research, currently focusing on microbial replication origins.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

In the last semester, how to balance teaching, research, editorial activities, and family life has been my biggest challenge, especially during the COVID-19 pandemic. The greatest achievement in my career is the systematic prediction of microbial replication origins using bioinformatics methods, some of which have been confirmed experimentally. The related web server Ori-Finder and online database DoriC have been gradually recognized by researchers in this field.

### 3. Why did you decide to become a board member?

A Nature Research journal launched in 2011, *Scientific Reports* is really a rising star with an experienced Chief Editor and renowned Editorial Board Members, and an editorial ethos unlike those of other Nature Research journals. This attracted me to become a board member in 2013.

### 4. What do you like most about being a board member for *Scientific Reports*?

I really enjoy the process of handling manuscripts from all over the world, which report the latest findings from the scientific community. I pick qualified manuscripts using rapid,

high-quality peer review, and present them to the readers in a timely manner. It's an excellent experience to see that the handled manuscripts were well-received by a wide audience or highly cited, which gives me a great sense of achievement.

### 5. What is your favourite *Scientific Reports* paper?

My favourite *Scientific Reports* paper is: 'RASTtk: A modular and extensible implementation of the RAST algorithm for building custom annotation pipelines and annotating batches of genomes', which has already been cited 570 times according to Web of Science. In fact, I often use the RAST server, which is a very popular genome annotation tool, to annotate our newly sequenced genomes. I was very glad to handle this manuscript and accept it for publication in *Scientific Reports* as quickly as possible.

## Professor Kenji Kansaku

*Professor Kenji Kansaku is a Professor and Chair at the Department of Physiology, Dokkyo Medical University School of Medicine, Japan. He is also an Editorial Board Member for* Scientific Reports *and Guest Editor for the 'Neuroprosthetics in systems neuroscience and medicine' Collection.*

### 1. What is your current research focused on?

I am a Systems Neuroscientist. I began my career as a neurosurgeon and, therefore, my research interests include both understanding brain functions and applying neuroscientific knowledge to medical practice. I am more specifically focused on practical neuroprosthetics, as well as neural mechanisms of body image and sense of self.

### 2. What has been your biggest challenge and your greatest achievement in your career so far?

Over the past 15 years, I have mainly focused on the brain–machine interface, which is a neuroprosthetic for patients with neurological disorders. Five years ago, I co-edited a book entitled "Clinical Systems Neuroscience" (Springer), which gathered chapters authored by researchers from various fields, including systems neuroscience, rehabilitation, neurology, psychology, and engineering.

### 3. Why did you decide to become a board member?

I felt that it would be an opportunity to contribute to various research fields worldwide.

### 4. What do you like most about being a board member for *Scientific Reports*?

*Scientific Reports* is unique in that it accepts articles with the only requirements being that they should be technically sound original contributions, and there is no focus on perceived importance and significance. Although the strategy may make it difficult for the journal to set research trends, it provides fair opportunities for papers that would otherwise potentially remain hidden for various reasons.

### 5. You are leading one of our Guest Edited Collections. What interested you about becoming a Guest Editor? What is your Collection focused on?

I am editing the Guest Edited Collection: Neuroprosthetics in Systems Neuroscience and Medicine. This Collection provides a platform for interdisciplinary research in neuroprosthetics, and gathers studies investigating medical applications of systems neuroscience, informatics, and engineering in the development of neuroprosthetic devices. As mentioned above, I edited a book 5 years ago entitled "Clinical Systems Neuroscience," in which all authors of the provided chapters were assigned by the editors. Here, the free submission style of the Collection has successfully gathered wonderful papers from various research fields. I would be happy for it to contribute to the development of a new special interest group worldwide.

Scientific Reports (*Sci Rep*) | ISSN 2045-2322 (online)

scientific reports



# Research articles

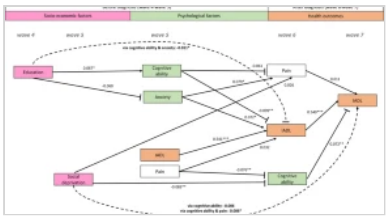
**Article Type**

**Article (21831)**

**Year**

**2022 (21831)**

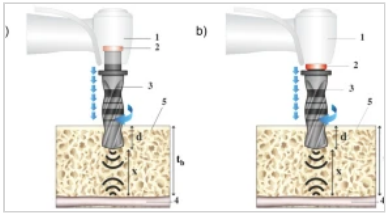
## The association of socio-economic and psychological factors with limitations in day-to-day activity over 7 years in newly diagnosed osteoarthritis patients



Afroditi Kouraki, Tobias Bast ... Ana M. Valdes

**Article** | Open Access | 18 Jan 2022

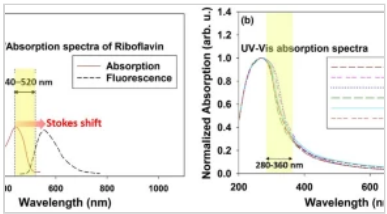
## Feasibility analysis of an ultrasound on line diagnostic approach for oral and bone surgery



Maria Alessandra Cutolo, Carlo Cafiero ... Antonello Cutolo

**Article** | Open Access | 18 Jan 2022

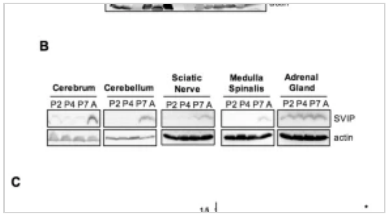
## Assay of honey freshness by a novel optical technique




Alireza Mashhadi, Ali Bavali & Farzad Mokhtari

**Article** | Open Access | 18 Jan 2022

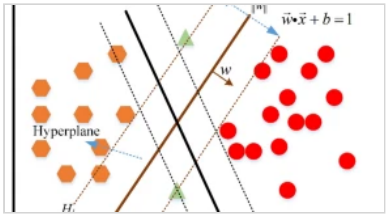
## Novel regulation mechanism of adrenal cortisol and DHEA biosynthesis via the endogen ERAD inhibitor small VCP-interacting protein




Recep Ilhan, Göklem Üner ... Petek Ballar Kirmizibayrak

**Article** | Open Access | 18 Jan 2022

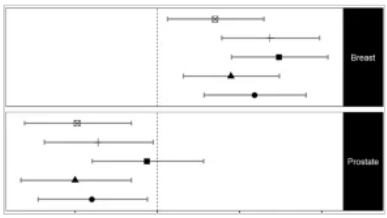
## Rock mass classification prediction model using heuristic algorithms and support vector machines: a case study of Chambishi copper mine




Jianhua Hu, Tan Zhou ... Pengli Huang

**Article** | Open Access | 18 Jan 2022

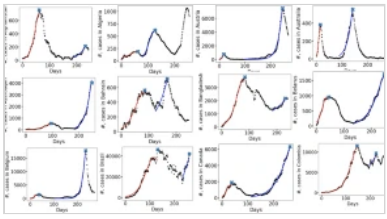
## Mendelian randomisation analyses of UK Biobank and published data suggest that increased adiposity lowers risk of breast and prostate cancer




Hasnat A. Amin, Pimpika Kaewsri ... Fotios Drenos

**Article** | Open Access | 18 Jan 2022

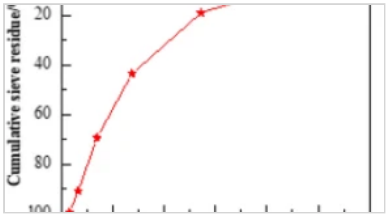
## Harnessing Artificial Intelligence to assess the impact of nonpharmaceutical interventions on the second wave of the Coronavirus Disease 2019 pandemic across the world



Sile Tao, Nicola Luigi Bragazzi ... Jude Dzevela Kong

**Article** | Open Access | 18 Jan 2022

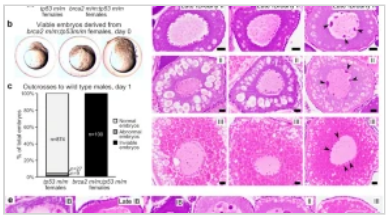
## Effect of nano-$SiO_2$ and nano-$CaCO_3$ on the static and dynamic properties of concrete




Zhi-hang Wang, Er-lei Bai ... Jing-sai Zhu

**Article** | Open Access | 18 Jan 2022

## *brca2*-mutant zebrafish exhibit context- and tissue-dependent alterations in cell phenotypes and response to injury



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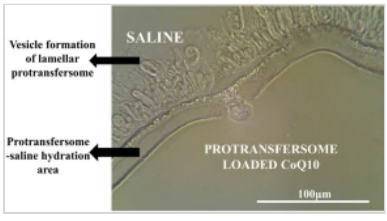
## Improving the anti-ageing activity of coenzyme Q10 through protransfersome-loaded emulgel




Qurrota Ayunin, Andang Miatmoko ... Djoko Legowo

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# Improving the anti-ageing activity of coenzyme Q10 through protransfersome-loaded emulgel

Qurrota Ayunin[1,2], Andang Miatmoko[3]✉, Widji Soeratri[3], Tristiana Erawati[3], Joni Susanto[4] & Djoko Legowo[5]

**Coenzyme Q10 (CoQ10) is a naturally produced organic molecule which acts as an antioxidant agent, including in skin anti-ageing, and plays a major role in the social determinants of health. However, its level in the body will decrease during ageing. Therefore, an external supplement is required to repair damaged skin, especially the skin dermis layer. This study aims to evaluate the use of a protransfersomal emulgel to improve the skin delivery and stability of CoQ10 which demonstrates low water solubility, poor permeability and instability. CoQ10 was initially dissolved in oleic acid at a weight ratio of 1:56. Protransfersome was then loaded with CoQ10 (Protransf-CoQ10) and prepared using a composition of L-α-Phosphatidylcholine and Tween 80 at a molar ratio of 85:15. The Protransf-CoQ10 was dispersed in an emulgel base consisting of Tween 80 and Span 80 to produce Protransf-CoQ10 emulgel. The in vivo studies of anti-aging activity and irritability were further evaluated by applying daily 200 mg of emulgels twice a day to a 4 $cm^2$ section on the back of a UV-ray aging-induced male Balb/c mouse 20 min before irradiation. The results showed that Protransf-CoQ10 could transform into transfersomal vesicles with particle sizes of approximately 201.5 ± 6.1 nm and a zeta potential of − 11.26 ± 5.14 mV. The dispersion of Protransf-CoQ10 into emulgel base resulted in stable Protransf-CoQ10 Emulgel during 28 days of observation at low temperatures. Moreover, the in vivo study revealed that Protransf-CoQ10 Emulgel successfully increases the collagen density and number of fibroblast cells in UV radiation skin-aged induced-mice which reflects its potential for repairing the skin ageing process. In addition, the 24-h topical application of Protransf-CoQ10 Emulgel showed that no erythema or skin rash was observed during the study. In conclusion, loading CoQ10 into protransfersomal Emulgel successfully enhanced the stability and anti-ageing efficacy enabling its potential use as anti-ageing cosmetics.**

Premature skin ageing occurs because the skin, as the outermost organ, is always directly exposured to oxidants in the environment and is frequently a determining factor in social life. In addition, with increasing age, the activity of mitochondria in the body as a producer of energy in regenerating cells and tissues decreases[1]. Both these internal and external factors cause impaired tissue function and structural changes[2] culminating in skin ageing characterized by thinning of the epidermis and skin dermis and, ultimately, resulting in wrinkles, fine facial lines, and loss of elasticity[3,4]. Skin elasticity is largely dependent upon young collagen fibers and fibroblasts, collagen-producing cells in the dermis layer, whose numbers decrease during the ageing process[5].

Anti-ageing cosmetics have been widely used to promote skin regeneration, especially of the upper skin layers which protect the skin against dehydration, penetration by various microorganisms, allergens, irritants,

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reactive oxygen species (ROS) and radiation, thereby maintaining healthy skin[6]. Coenzyme Q10 (CoQ10) is one of the natural compounds often employed as an antioxidant, which plays a key role in stabilizing plasma and other intracellular membranes that protect against membrane phospholipid peroxidation[7]. CoQ10 acts by maintaining skin quality against free radicals[3] which have been known to activate the mitogen-activated protein kinase (MAPK) pathway that produces matrix metalloproteinases (MMPs) such as collagenase, thus damaging collagen fibers[8–10]. During ageing, the levels of CoQ10 in organs, including the skin, also decrease with the result that it is necessary to supply CoQ10 to achieve normal levels of between 0.50 and 1.65 μg/mL within the body. Topical administration of CoQ10 has been shown to be effective in reducing wrinkles in skin that has been exposed to UV rays[3].

CoQ10 demonstrates low solubility in water (0.193 μg/mL) with a large molecular weight of 863.36 g/mol and high lipophilicity with a log P value of 21. This limits its penetration of the skin and explains it tendancy to be deposited in the stratum corneum[11,12]. Moreover, CoQ10 decomposes when exposed to light[13]. Loading CoQ10 into protransfersome, a vesicular carrier would probably constitute an effective strategy to enhance its biological activity within the skin in addition to increasing its stability.

Protransfersome, one of the provesicular nanocarriers that provides superior skin penetration and high stability, is widely used in transdermal delivery[14]. It possesses a flattened liquid crystal structure which is converted into an ultraflexible vesicle known as transfersome through the absorption of water from the skin during in situ hydration[15–17]. Transfersome is known to be an ultradeformable vesicle which is highly flexible and deformable, rendering it capable of passing through three skin penetration pathways[18]. Transfersome can rapidly penetrate the stratum corneum and enter the deeper skin layers via the intercellular lipid of the stratum corneum. It can fuse with the cell membrane, enabling it to enter the transcellular pathway, and is able to penetrate intact through the hair follicle pathway to penetrate the deeper layers of the skin[19–21]. Protransfersome is composed of amphiphatic lipid components such as phosphatidylcholine which, significantly, form double-layer membrane of vesicles, and surfactant as an edge activator that increases the vesicle flexibility or deformability[22]. In general, protransfersome contains a larger number of phospholipids than that present in transfersomes. During the manufacturing process, the protransfersome does not undergo an extrusion process to produce unilamellar vesicles as observed in the transfersome. This is because the protransfersome is a provesicular carrier system which will be converted into transfersome after it comes into contact with water in situ[23]. Therefore, under a light microscope, the protransfersome can be seen to possess a palisade crystalline liquid form, whereas transfersomes are vesicular when in liquid media[24].

The use of ultradeformable vesicles has successfully improved the skin penetration of drugs and efficacy of anti-ageing properties of certain antioxidant molecules such as tocopherol which, when prepared in transfersome, possess good characteristics with a particle size < 100 nm and entrapment efficiency of up to 90%. Moreover, it is well distributed within the skin layer and in vitro tests have proved it biocompatible with keratinocytes and fibroblasts, indicating its protective effect against oxidative damage and the potential for wound healing[25]. Previous reports have evaluated the use of nanocarriers for CoQ10 delivery such as a self-emulsifying drug delivery system (SEDDS)[26], ethosomes[27], transethosomes[28], and microemulsion[29]. The use of transethosomes successfully encapsulated CoQ10 up to 97% in vesicles and produced > 95% drug deposition in different skin layers resulting in high efficacy for androgenic alopecia[28]. The low water solubility of CoQ10 frequently limits drug encapsulation efficiency in nanocarriers, thus the use of large amounts of lipid phase or ethanol may improve its loading.

In this study, a protransfersome containing CoQ10 will be prepared for anti-ageing emulgel. The high level of phospholipids contained in protransfersome is intended to improve drug loading. The use of protransfersome in the anti-ageing activity and irritation level of Protransf-CoQ10 emulgel was evaluated in vivo using UV-induced aged mice models. This study could represent an attempt to improve CoQ10 anti-ageing activity with the result that is effective, safe and non-irritating.

## Results

This study aims to evaluate the potential use of protransfersome for topical delivery of CoQ10 as an anti-ageing agent. This study provides a scientific approach to successfully delivering low water solubility and poor permeable lipophilic substances and nanovesicular carriers specifically designed for anti-ageing cosmetics. The CoQ10 was loaded into protransfersomal emulgel composed of oleic acid containing soluble CoQ10, phospholipids as bilayer-forming lipids, and Tween 80 which acts as the edge activator of bilayer membrane after the protransfersome has been hydrated with skin water in situ, before being loaded into an emulgel base. There were improvements in stability and potential efficacy to inhibit premature ageing of the skin in UV-radiation skin aged-induced mice models as demonstrated in this study.

**Physical characteristics and stability of protransfersome-loaded CoQ10 emulgel.** After dissolving the CoQ10 in oleic acid and encapsulated it into protransfersomes composed of phospholipids and Tween 80, the protransfersome-loaded CoQ10 (Protransf-CoQ10) forms a bright orange, viscous, oily liquid, with a distinctive phospholipid smell, and viscous consistency. After hydration with saline, lamellar vesicular structures rapidly formed and were ultimately transformed into transfersome vesicles, as shown in Fig. 1.

The dispersion of Protransf-CoQ10 into the emulgel base (Fig. 2A, B) at a weight ratio of 2:1 produced Protransf-CoQ10 Emulgel whose color changes to brownish orange with a reduction in its pungent smell as shown in Fig. 2C. CoQ10 dissolved in oleic acid (CoQ10-Ole) was in the form of a bright orange odorless emulgel (Fig. 2D) whose character is identical to that of CoQ10 Emulgel except that it is more transparent due to no oleic acid being present in the formula (Fig. 2E). The darkening color of Protransf-CoQ10 emulgel probably due to large amount of L-α-Phosphatidylcholine content of which is dark yellow in color[30] and easily oxidized when it is exposed to air in for lengthy periods[31,32].

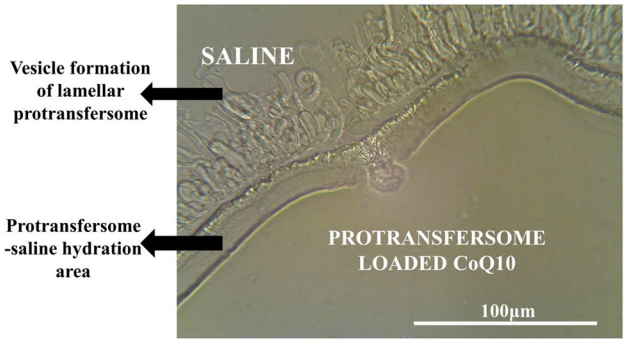


**Figure 1.** Lamellar structure of liquid crystals of the CoQ10 protransfersome emulgel after adding one drop of saline under an optical microscopy observation at ×400 magnification (Scale bar:100 µm).

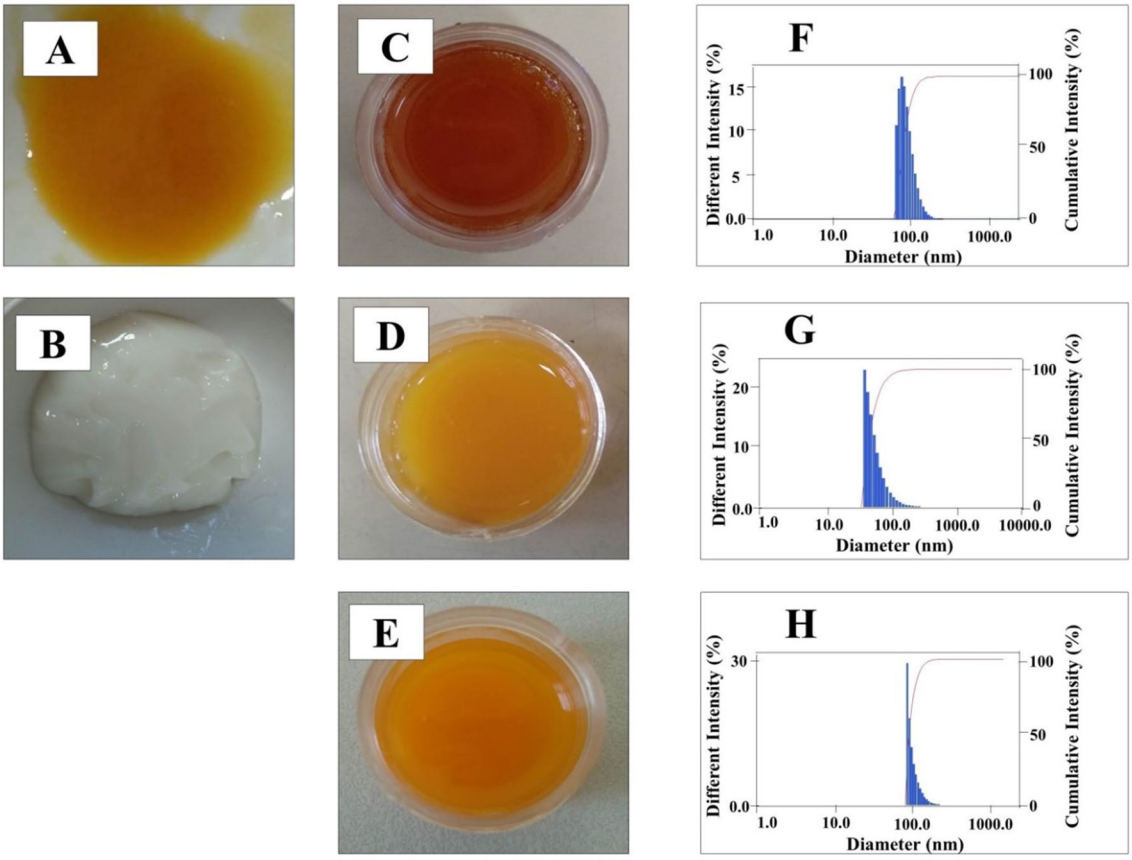


**Figure 2.** Visual appearance of protransfersomal CoQ10 (Protransf-CoQ10) (**A**), emulgel base (**B**), protransfesomal CoQ10 (Protransf-CoQ10) Emulgel (**C**), CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel (**D**), and CoQ10 loaded in emulgel (CoQ10 Emulgel) (**E**). The Intensity distribution of particle of protransfesomal CoQ10 (Protransf-CoQ10) Emulgel (**F**), CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel (**G**), and CoQ10 loaded in emulgel (CoQ10 Emulgel) (**H**).

The particle size and polydispersity index value were further evaluated since they determine the ability of the vesicles to penetrate the deeper layers of the skin. The smaller the particle size of the vesicles, the easier the vesicles are to penetrate. In addition, the smaller the polydispersity index value, the more homogeneous the particle size of the vesicles[17], thus ensuring that a larger number of vesicles penetrate the skin. From the results, it is evident that the entrapment efficiency value of the CoQ10 in Protransf-CoQ10 is comparatively high at 45.64 ± 7.52% with particle size of 201.5 ± 6.1 nm (by manual shaking method), polydispersity index value of 0.229 ± 0.047, and ζ-potential of − 11.26 ± 5.14 mV, as presented in Table 1. The manual shaking method of 5 min duration was reflective of the real situation in which protransfersomes change into transfersomes. The Protransf-CoQ10 Emulgel had the smallest particle size compared to both CoQ10-Ole Emulgel and CoQ10 Emulgel, which were 134.3 ± 4.8 nm < 146.9 ± 1.6 nm < 238.8 ± 3.1 nm, respectively, with intensity distribution

| Formula | Particle size (nm) | Polydispersity index (PDI) |
|---|---|---|
| CoQ10 Emulgel | 238.8 ± 3.1 | 0.384 ± 0.010 |
| CoQ10-Ole Emulgel | 146.9 ± 1.6 | 0.298 ± 0.019 |
| Protransf-CoQ10 Emulgel | 134.3 ± 4.8 | 0.291 ± 0.020 |

**Table 1.** Particle Size and polydispersity index of CoQ10 loaded in emulgel (CoQ10 Emulgel), CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel, and protransfesomal CoQ10 (Protransf-CoQ10) Emulgel. Each value represents the mean ± SD (n = 3).

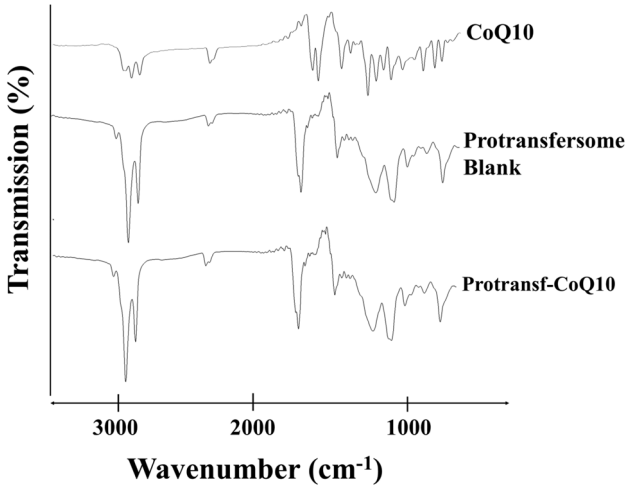


**Figure 3.** Fourier-transform infrared spectra of Coenzyme Q10 (CoQ10), Blank protransfersome, and protransfersome loaded CoQ10 (Protransf-CoQ10).

of particle presented in Fig. 2F–H. The polydispersity index values for Protransf-CoQ10 Emulgel, CoQ10-Ole Emulgel, and CoQ10 Emulgel were 0.291 ± 0.020 < 0.298 ± 0.019 < 0.384 ± 0.010.

In order to evaluate any interaction between CoQ10 and protransfersomal matrix, a Fourier Transform Infra Red (FTIR) analysis was further observed. As presented in Fig. 3, there were no new absorption bands of functional groups or peak shifts observed for Protransf-CoQ10, which shows similar infrared spectroscopical profiles to Protransfersome blank, while no specific peaks of CoQ10 appear. This result indicates that CoQ10 successfully encapsulated protransfersome and no chemical interaction between the mixtures occurred[33–35].

Moreover, according to the result of differential thermal analysis, the CoQ10 encapsulation into protransfersome produced changes in the structure of cristallinity. CoQ10 and L-α-Phosphatidylcholine showed sharp endothermic peaks at 53.3 and 112.3 °C, respectively; however, protransfersomal CoQ10 showed weak endothermic peak at 143.9 °C indicating that less ordered crystalline structures were observed as presented in Fig. 4.

A physical stability test was subsequently carried out to determine the physical resistance of the system when stored at different temperatures, namely; room temperature and a lower temperature for 28 days. During the study, the parameters of particle size, polydispersity index, and pH were observed. As seen from Fig. 5, the results showed that after a 28-day storage period, there were no significant differences in particle size or polydispersity index ($P < 0.05$). On the other hand, a significant difference was observed in the pH during the same period, although the pH value remained within the pH range of the skin. No significant difference existed in the particle size or particle size distribution of the preparation after 28 days of storage.

**In vivo anti-ageing activity of protransfersome-loaded CoQ10 emulgel.** To evaluate the ability of protransfersomes to topically deliver CoQ10 and produce an effective anti-ageing activity, the Protransf-CoQ10 Emulgel was topically applied for 14 days to the back skin of UV-rays-induced subjects who were subsequently observed for skin histopathology. The control group subjects which received UV rays had the lowest collagen density of 52.30 ± 7.87%, indicating that UV rays damage the collagen in the skin dermis. The administration of both Protransf-CoQ10 Emulgel and CoQ10-Ole Emulgel significantly improved the collagen density of UV-ray radiated subjects' skin as indicated in Fig. 6. However, there was no significant difference between these groups. The use of protransfersomes successfully delivered CoQ10 providing protection against skin damage and repaired that resulting from exposure to UV rays.

The anti-ageing activity test result was further analyzed by observing the number of fibroblast cells capable of producing collagen. Therefore, the higher the number of fibroblasts, the more collagen was formed. In this study, the assessed fibroblasts were young and light purple in appearance. The results showed that the CoQ10 Emulgel had a significantly different number of fibroblasts compared to the control group, with pro-CoQ10

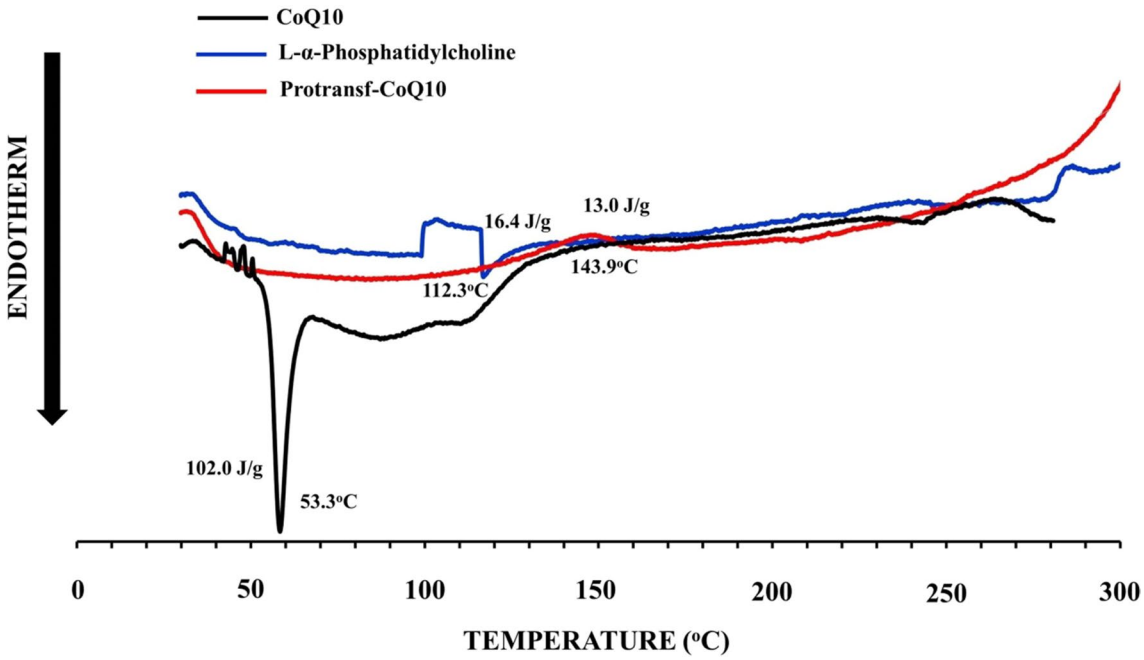


**Figure 4.** Differential thermal analysis of Coenzyme Q10 (CoQ10), L-α-Phosphatidylcholine as phospholipid component of protransfersome, and protransfersome loaded CoQ10 (Protransf-CoQ10).

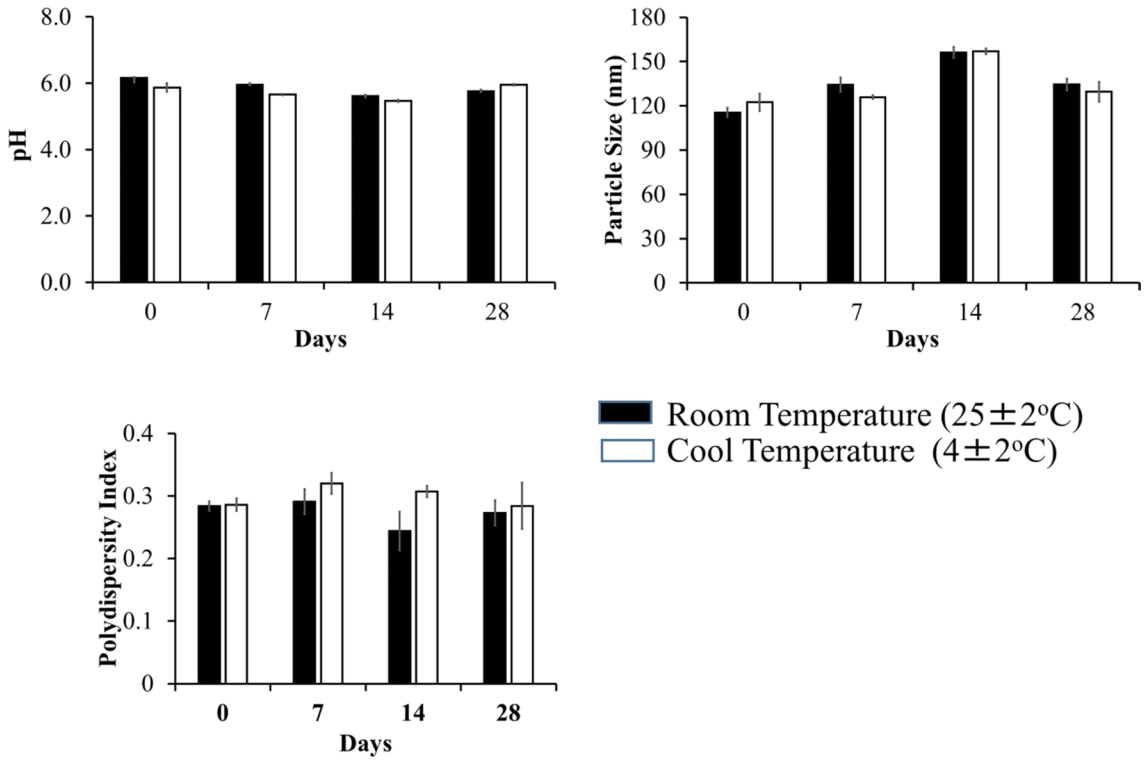


**Figure 5.** Evaluation of particle size, polydispersity index, and pH stability of protransfersomal CoQ10 loaded in emulgel (Protransf-CoQ10 Emulgel) during 28 days stored at room (25 ± 2 °C) and cool (4 ± 2 °C) temperatures.

Emulgel producing the highest number of fibroblasts, which was 31.50 ± 9.48 cells per field view, as indicated in Fig. 7. This shows that protransfersomes delivering CoQ10 successfully increase the number of fibroblasts.

**In vivo skin irritation test.** The safe use of Protransfersome-loaded emulgels in this study was also evaluated by conducting an in vivo irritation test. Epidermis liquefaction, subepidermis edema, collagen fiber swell-

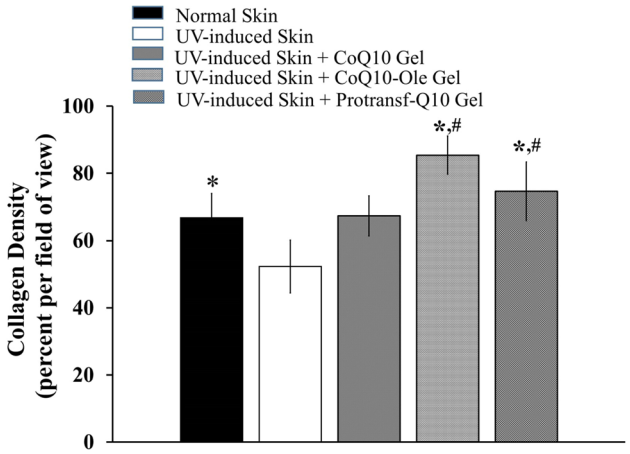


**Figure 6.** The collagen density of dermis layer of subject's back skin without and with UV-induced photoageing after topically applied with saline (Normal skin and UV-induced skin), CoQ10-loaded Emulgel, CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel, and protransfesomal CoQ10 (Protransf-CoQ10) Emulgel once every 2 days for 2 weeks. *$P<0.05$ compared to UV-induced skin, #$P<0.05$ compared to Normal Skin.

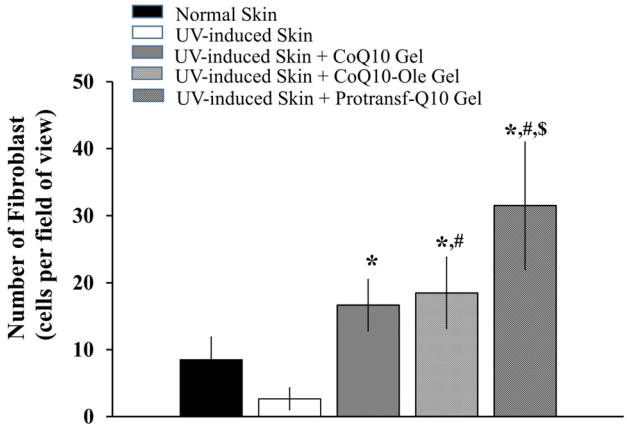


**Figure 7.** The number of fibroblasts of mice back skin without and with UV-induced photoageing after topically applied with saline (Normal skin and UV-induced skin), CoQ10-loaded Emulgel, CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel, and protransfesomal CoQ10 (Protransf-CoQ10) Emulgel once every 2 days for 2 weeks. *$P<0.05$ compared to UV-induced skin, #$P<0.05$ compared to Normal Skin, \$ $P<0.05$ compared to CoQ10-Ole treated skin.

ing, inflammatory cells infiltration, dan appendages degeneration were observed for determining irritation in model's skin. As presented in Fig. 8, there are differences in skin histopathology between normal and UV-induced skin. For further evaluation of severity level of skin irritation, scoring was then determined for each group.

The results of the histopathological scoring of the models' back skin after 24 h of application showed that CoQ10 Emulgel had an irritation score of 0.52, while CoQ10-Ole Emulgel had one of 1.36, and Protransf-CoQ10 Emulgel one of 0.92 as presented in Fig. 9. This result shows that the Protransf-CoQ10 Emulgel does not irritate the skin, while the CoQ10-Ole Emulgel induced mild irritation due to the nature of oleic acid. According to the Kruskall Wallis statistical test results, there was no significant difference between these emulgel preparations.

## Discussion

In this study, the Protransfersomes and Protransfersomal emulgel preparations for CoQ10 delivery as the active cosmetic ingredient have the potential to inhibit premature ageing of the skin. The main purpose of protransfersome formulation is to significantly encapsulate CoQ10 in order to modify the physicochemical characteristics of CoQ10, rendering it more water dispersible and able to penetrate the skin since high lipophilic CoQ10 demonstrates low water solubility and poor skin penetration. However, the high content of oleic acid, which accounted for approximately 37% of the final weight of protransfersomal emulgel, would render it unacceptable for daily use as a skin cosmetic. Therefore, it was added to emulgel to increase its appropriateness for use. As far as the functional aspects of vesicles are concerned, the formation of transfersome due to hydration of protransfersome

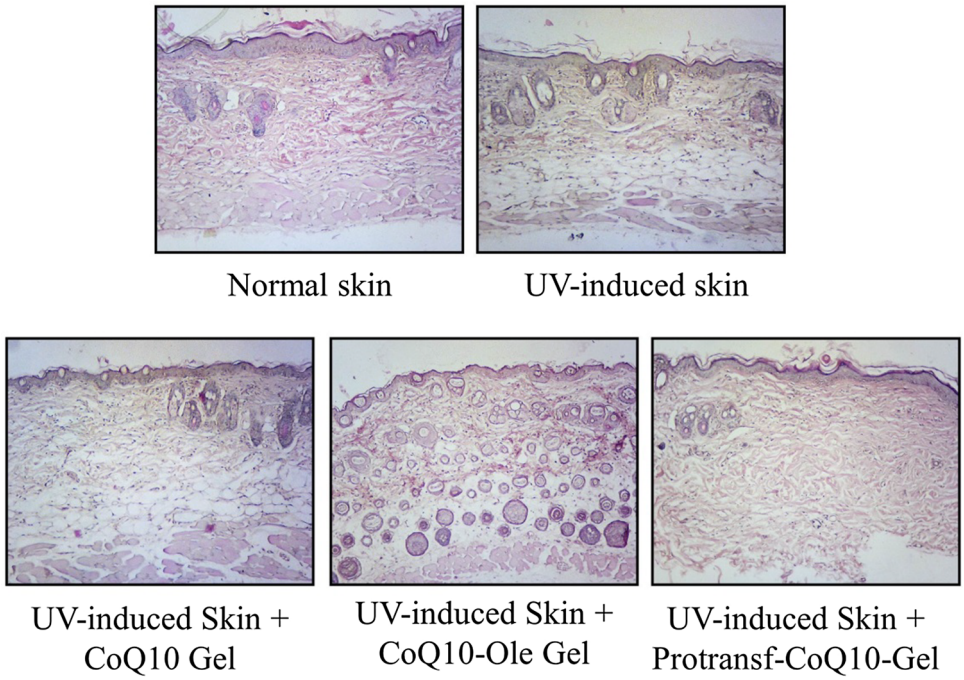


**Figure 8.** The histopathology of mice back skin stained with hematoxylin–eosin without and with UV-induced photoageing at 24 h after topically applied with saline (Normal skin and UV-induced skin), CoQ10-loaded Emulgel, CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel, and protransfesomal CoQ10 (Protransf-CoQ10) Emulgel.

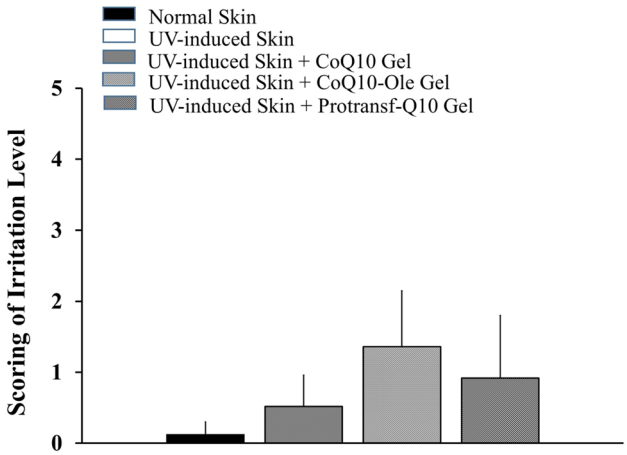


**Figure 9.** The scoring results of histopathology of mice back skin s without and with UV-induced photoageing at 24 h after topically applied with saline (Normal skin and UV-induced skin), CoQ10-loaded Emulgel, CoQ10 dissolved in oleic acid (CoQ10-Ole) Emulgel, and protransfesomal CoQ10 (Protransf-CoQ10) Emulgel.

by water content in the emulgel base produces ultra-deformable vesicles which allow them to easily penetrate the skin. In addition, previous reports showed that the presence of a gelling agent would act as a steric hindrance which would be adsorbed onto the vesicle surface preventing fusion or aggregation, thus increasing physical stability during storage[36,37]. The addition of lipid vesicles to gel is beneficial for increasing vesicle stability, prolonging drug release, improving dermal permeability, and enhancing drug deposition in the skin[38].

Protransfersomes have been developed as the nanometer-sized carrier form of transfersome provesicles and have a higher phospholipid content compared to transfersomes. This enables the protransfersome system to demonstrate greater entrapment efficiency due to a higher number of vesicles formed that are subsequently available for encapsulating drugs, thus providing high stability when compared to the transfersome system[24]. Protransfersomes are able to carry active ingredients through the skin pores into the deeper layer. The protransfersome system analyzed in this study has positive characteristics including nanometer size, and thick consistency

resulting from its large phospholipid content. When the protransfersome is observed using a light microscope, a palisade lamellar structure appears in the form of liquid crystals. This is due to differences in the degree of hydration of surfactants and phospholipid molecules triggered by solvent limitations. The protransfersome forms as a mixture of flat liquid crystals resembling palisade and vesicular lamellae linked together[39]. The percentage of entrapment efficiency (EE%) of the protransfersome system is a parameter used to predict the stability of the dispersion[40] describing the amount of drug present in the vesicle[41]. In this study, the EE% value was comparatively large because it corresponded to the phospholipid content in the formula[42] and the tendency of CoQ10 to be retained in the phospholipid membrane due to its lipophilic properties[39].

To improve acceptability, the protransfersome was formulated as an emulgel preparation incorporating the use of an emulgel as the gel base. In this study, three types of emulgels were developed and evaluated for their anti-ageing and irritability activity, namely; Protransf-CoQ10 emulgel, emulgel loaded CoQ10 which was previously dissolved in oleic acid (CoQ10-Ole emulgel) and CoQ10 dispersed in an emulgel base (CoQ10 emulgel).

During the homogenization method for preparing necessary samples the particle size test involves manual shaking which is considered to closely replicate real-life conditions. The particle size of the emulgel loaded Co-Q10 remained in the nanometer range, indicating that adding emulgel base to the particle size of Protransf-CoQ10 had no effect. The particle size of Protransf-CoQ10 Emulgel is smaller than that of Protransf-CoQ10 itself. This indicates that the particles have turned into transfersome vesicles because they have been partially hydrated by the presence of water in the emulgel base. The decreased vesicle size of protransfersomal CoQ10 after dispersion into the emulgel base is probably due to the shearing stress that occurs during the incorporation of Protransf-CoQ10 into hydrated Carbopol-based emulgel. This causes the small vesicles formed and the emulgel matrix to be adsorbed onto the vesicle surface, preventing vesicle fusion or aggregation[36,37], while spontaneous hydration of protransfersome produces larger vesicles than those resulting from dispersion into emulgel. When compared to the particle sizes of CoQ10-Ole Emulgel and Co-Q10 Emulgel, those of all three emulgels-loaded CoQ10s can be measured in nanometers. The order of particle size from the smallest to the largest is Protransf-CoQ10 Emulgel < CoQ10-Ole Emulgel < Co-Q10 Emulgel. Co-Q10 Emulgel is the largest in size because CoQ10 is only dispersed in the emulgel base, while Protransf-CoQ10 Emulgel and CoQ10-Ole Emulgel had similar particle size and PDI probably due to CoQ10 solubility in Oleic Acid for both formulas[43]. From the results of the polydispersity index, it is evident that all particles have a uniform size distribution. This indicates that the preparation will be stable during storage because it reduces the tendency for particle aggregation which causes the system to become unstable.

A test was carried out to determine the physical stability of Protransf-CoQ10 emulgel when stored at different temperatures, namely; room temperature and colder temperatures for 28 days and whether differences in particle size, polydispersity index, and pH existed. There was no significant difference in particle size, polydispersity index, and pH of Protransf-CoQ10 emulgel during the study period.

The results of the anti-ageing activity of CoQ10 loaded in emulgel and evaluated for skin collagen density confirmed CoQ10-Ole Emulgel as having the highest percentage of collagen density, followed by Protransf-CoQ10 Emulgel. However, no significant difference existed between these groups ($P > 0.05$). These two groups demonstrated significant improvement in collagen density compared with the control group whose subjects had been exposed to UV and who recorded the lowest density value. This is probably due to soluble CoQ10 in Oleic Acid loaded into emulgel had been easily released from emulgel than that of Protransf-CoQ10 Emulgel, which the formation of vesicle during hydration results in semipermeable bilayer membrane as water diffusion-limiting barriers for CoQ10 release. The low collagen density has been known caused by imbalance between collagen synthesis by fibroblasts and collagen degradation of UV irradiation, while collagen synthesis is proportionally relate to fibroblasts resident[44]. Moreover, collagen synthesis by fibroblast will actively occur on the 4th day of 21 days[45]. The faster CoQ10 release from CoQ10 Ole Emulgel will stimulates fibroblast proliferation which increase expression of collagen matrix[46], while the late CoQ10 release from Protransf-CoQ10 Emulgel will result in delayed effects on fibroblast-stimulated collagen synthesis.

On the other hand, the Co-Q10 Emulgel-treated group had similar collagen density to that of normal mice, indicating that UV light damages collagen in the skin dermis. It has been known that UV-irradiation damage dermal collagen and elastin fibers[47], while CoQ10 increased the collagen content through decrease of MMP-1 protein level in mice exposed with UV-B[48]. CoQ10 also promotes the fibroblast proliferation[49]. However, it seems that the fibroblast stimulation process to produce collagen matrix between normal and CoQ10-treated groups is different. This situation differed from that of the group treated with CoQ10 in the emulgels. From these results, it can be concluded that CoQ10 provides protection against the ageing effects of UV rays.

The anti-ageing activity test was further evaluated for the number of fibroblasts in the skin tissues. Fibroblasts are cells capable of producing collagen. In this case, the assessed fibroblasts were young and light purple in color. The higher the number of fibroblasts, the more collagen was formed. The results showed that the CoQ10 emulgels had a significantly different number of fibroblasts compared to the control group, with the Protransf-CoQ10 Emulgel having the highest number, which was $31.50 \pm 9.48\%$ per field view. This indicates that CoQ10 is able to increase the number of fibroblasts.

The safety of these anti-ageing emulgels was further evaluated by an irritancy test. The results indicated that the Protransf-CoQ10 Emulgel produced no signs of irritation in the skin tissues observed, while the CoQ10-Ole Emulgel induced mild skin irritation due to the nature of oleic acid.

Protransf-CoQ10 Emulgel has potential as an anti-aging product. However, information is lacking about both the drug release profile and its dermal penetrability which supports the theory that protransfersome and its incorporation into emulgel could prove a useful model for developing skin anti-aging cosmetics. Moreover, both the ability of protransfersome and protransfersomal emulgel to maintain drug stability and the physicochemical properties of the forms of skin dosage need to be evaluated for drug levels during study periods in line with ICH guidelines. Therefore, the product development involved could be comprehensively analyzed.

| Component | Amount in formula (%) | | |
|---|---|---|---|
| | Protransf-CoQ10 Emulgel | CoQ10-Ole Emulgel | CoQ10 Emulgel |
| Coenzyme Q10 | 1.0 | 1.0 | 1.0 |
| L-α-Phosphatidylcholine | 24.9 | – | – |
| Oleic acid | 37.2 | 37.2 | – |
| Tween 80 | 4.3 | 4.3 | – |
| Emulgel base | Up to 100.0 | Up to 100.0 | Up to 100.0 |

**Table 2.** Formulation of CoQ and protransfersomal CoQ10-loaded emulgels.

## Conclusions

The results of this study indicate that emulgel-loaded protransfersomes, employed as delivery carriers of CoQ10, possess positive physical properties, thereby increasing anti-ageing activity with a low skin irritancy score. Proposing the incorporation of protransfersomal emulgel into cosmetics requires further studies especially on the acceptability test in humans and stability tests for longer storage times. From the results of this study, although the primary nature of CoQ10 severely limits its skin delivery, protransfersome provides potential benefits when used as a delivery system for active cosmetic ingredients within skin ageing therapy.

## Methods

**Materials.** In this study Coenzym Q10 (CoQ10) was obtained from Kangcare Bioindustry Co. Ltd. (Nanjing, China). L-α-Phosphatidylcholine is a product of Sigma-Aldrich (Buchs, Switzerland). Tween 80 and Span 80 were both purchased from Enviro Prima Co. Ltd. (Tangerang, Indonesia). The oleic acid used in this study was acquired from Brataco Co. Ltd. (Surabaya, Indonesia). All other reagents were of the available pharmaceutical and analytical grades.

**Preparation of CoQ10-loaded protransfersome (Protransf-CoQ10).** The protransfersome was composed of L-α-Phosphatidylcholine, Oleic Acid, and Tween 80 as shown in Table 2 and prepared with modifications by the method previously reported by Gupta (2012)[16]. Initially, CoQ10 was stirred until completely dissolved in a mixture of oleic acid and Tween 80. Finally, L-α-Phosphatidylcholine was added and stirred until dissolved to produce Protransf-CoQ10.

**Preparation of emulgel containing CoQ10-loaded protransfersome (Protransf-CoQ10 Emulgel).** A CoQ10-loaded protransfersome emulgel was prepared by adding the Protransf-CoQ10 to the emulgel base with a final CoQ10 content of 1%. The emulgel base was produced using Carbopol 940 added to a combination of Tween 80 and Span 80 (1:1) to form a homogenous emulgel base with the addition of Triethylamine (TEA) to adjust the pH to 6.0 ± 0.2. Protransf-CoQ10, CoQ10 solution in oleic acid, and CoQ10 powder were subsequently added to this emulgel base and mixed homogenously to produce Protransf-CoQ10 emulgel, CoQ10-Ole emulgel, and CoQ10 emulgel, respectively.

**Evaluation of physical characteristics.** The evaluation of physical characteristics includes particle size, polydispersity index, ζ-potential, microscopic observation, entrapment efficiency, and physical stability during storage.

The dispersion of Protransf-CoQ10 into an emulgel base at a weight ratio of 2:1 produced Protransf-CoQ10 emulgel whose color changes to brownish orange and the reduction on its pungent odor. Meanwhile, the CoQ10 dissolved in oleic acid (CoQ10-Ole) emulgel had an odorless, jelly-like consistency and was bright orange in color. These characteristics were identical to those of CoQ10 emulgel, although the latter had a more transparent appearance due to the absence of oleic acid from the formula.

Evaluation of particle size and ζ-potential were respectively carried out using a Delsa™ Nano Submicron Particle Size Analyzer (California, USA) and light scattering and electron scattering methods. Approximately 50 mg of CoQ10-loaded protransfersome and emulgels were resuspended in 5 mL of 0.9% NaCl. The samples were then prepared using the manual shaking method for 5 min[24]. The suspension was further diluted by pipetting 150 µL of sample and added with 2 mL of deionized water (Otsuka Indonesia, Lawang, Indonesia) for sample measurement.

The Protransf-CoQ10 was observed microscopically to evaluate its transformation ability in relation to transfersome vesicles by placing a small amount of sample on a glass slide and covering it with a cover glass. A drop of 0.9% NaCl saline solution was added to the other side of the cover slip's cavity[50]. The evaluation was conducted using an optical microscope before, during, and after addition of 0.9% NaCl at 400 × magnification.

The EE% was measured for CoQ10 loaded in protransfersome by means of UV–Vis spectrophotometry[17]. Approximately 100 mg of Protransf-CoQ10 was weighed, and then hydrated with 2 mL phosphate buffered saline (PBS) pH 7.4 and sonicated for 30 min until homogeneous. The suspension formed was then centrifuged at 3000 rpm for 30 min to obtain supernatant and sediment in a 10 mL glass tube. The sample was prepared by taking 1.5 mL of supernatant and then dissolved in 2 mL methanol, added to 2 mL PBS pH 7.4 and, finally, sonicated for 15 min. The sediment was dissolved in 1.5 mL methanol, added to 2 mL of PBS and sonicated for 15 min. The absorbance of each sample was measured by UV–Vis spectrophotometry at a wavelength of 275 nm. The EE (%) of CoQ10-loaded in protransfersome was calculated by means of the following equation:

$$\text{EE}\,(\%) = \frac{CoQ10\ levels\ in\ supernatant}{CoQ10\ levels\ in\ supernatant + CoQ10\ levels\ in\ sediment} \times 100\% \quad (1)$$

In order to evaluate whether any chemical or physical changes occurred in samples, spectroscopical and thermal analysis were further investigated. The spectroscopical analysis was evaluated using a Fourier Transformed Infra-Red analysis by using Spectrophotometer ECO ATRS Bruker Alpha II (Germany). About 1 mg sample was analyzed at wavenumbers of 450–4000 $cm^{-1}$. While, the thermal analysis was evaluated using *Differential Thermal Analysis* (DTA) instrument (Mettler Toledo FP 85, Switzerland). About 3–5 mg samples was put into crucible sample pan. The sample was then subsequently heated from 30 to 300 °C at a heating rate of 10 °C per minutes.

Moreover, a stability test of the Protransf-CoQ10 emulgel was carried out by storing the samples at in the dark at room temperature (24 ± 2 °C) and, subsequently, a cold temperature (4 ± 2 °C) for 28 days[51–53]. The emulgel was evaluated for physical characteristics, i.e., pH and particle size, on the 28th day after preparation.

**In vivo study of anti-ageing in UV-rays ageing induced mice.** The in vivo anti-ageing activity was evaluated using Balb/c mice (*Mus musculus*) within the terms of a study protocol approved by The Ethics Commission of Faculty of Veterinary Medicine, Universitas Airlangga (Certificate number 2.KE.016.02.2020 dated February 4, 2020). All methods were performed in accordance with ARRIVE guidelines and relevant regulations[54]. Within this research, two types of study involving the uses of experimental models were evaluated, firstly, anti-ageing activity as indicated by collagen density and number of fibroblasts, and, secondly, a safety test incorporating irritancy scoring of skin tissue. The effect of the Protransf-CoQ10 emulgel was compared with those of CoQ10-Ole and CoQ10 emugels. Each group comprises of 4 mice as the study model. Prior to the study, the hair on the models' backs was trimmed with mechanical hair clippers, ensuring that their skin was not injured during this process. Each model was housed in a separate cage to prevent their touching the part to be smeared with the sample.

**Anti-ageing activity test.** The anti-ageing activity test was evaluated to establish the parameters of collagen fiber density and the number of fibroblasts. The study was carried out by applying 200 mg of the emulgels twice a day every day to a 4 $cm^2$ area of previously shaved skin on the models' backs. The sample was applied 20 min before UV irradiation, in order to provide time for absorption into the skin, and four hours after irradiation which is the point at which the formation of Reactive Oxygen Species commences. An 80 $mJ/cm^2$ dose of UV light was administered at an irradiation distance of 15 cm for 21 min. UV irradiation was carried out once every 2 days, namely; on days 1, 3, 5, 7, 9, 11, and 13, with the models subsequently being left for 24 h on completion of the irradiation process to overcome the effects of acute irradiation[55]. Sample application was also conducted on days when the models were not exposed to UV irradiation. After 14 days, the models were sacrificed by dislocation with the skin tissues being subsequently excised to produce a tissue section using a microtome. To evaluate the collagen density, the tissue section was stained with Masson trichrome staining, while for the observation of fibroblasts, the skin tissue section was stained with Hematoxylin–Eosin Staining. The tissue section was then observed with a light microscope (Olympus CX 31 Camera DP 22) using Cellsen Standard Software. Collagen density was measured by histochemical scoring, while the number of fibroblasts was calculated by digital analysis using Adobe Photoshop and Image J software. Density measurement involved measuring the area of collagen coir and comparing it with the field of view. The denser the coir collagen, the higher the density value, and vice versa. Calculation of the density value was completed by means of calculating the area of the field of view and the black colored area using Image J software calibrated fin advance or each degree of magnification. The comparison of the black stained area with the field of view produced the density value.

**In vivo skin irritancy evaluation of proransfersome loaded CoQ10 in emulgels.** In order to observe the irritant effects of CoQ10-loaded in proransfersome and emulgels, histopathological changes in the skin tissues of each model after a 24-h period of exposure were observed. Firstly, the back hair of the models had been shaved. Approximately 200 mg of the sample was then applied to a 2 × 2 $cm^2$ area of skin on their backs. Twenty-four hours after application, the models were sacrificed by dislocation. Skin was excised with a microtome before being immersed in a formalin solution and stained with hematoxylin–eosin. The preparations were observed with a light microscope to assess the degree of skin irritation by means of histopathological scoring. Histological change data is semi-qualitative and features five variables, namely; epidermis liquefaction, subepidermal edema, collagen fiber swelling, inflammatory cell infiltration, and degeneration of the appendages in hair vesicles. The scoring method comprised a score of 0 = normal skin, 1 = mild irritation, 2 = moderate irritation, and 3 = severe irritation[56]. The data from each sample consisted of the mean value of the variable score for each of the five different fields of view at 100 × and 400 × magnification. All examinations involved the use of an ordinary light microscope (Nikon H600L, equipped with a 300 megapixel DS Fi2 digital camera and Nikkon Image System image processing software).

**Statistical analysis.** The data in this study consisted of three replicates. In order to test the significance of differences in the data relating to Protransf-CoQ10 emulgel, CoQ10-Ole emulgel, and CoQ10 emulgel, a statistical analysis was performed using the one-way variant analysis (ANOVA) method. After the normality and homogeneity of the data had been tested, a Post Hoc Tukey HSD test was administered. If the *P value* < 0.05, then a significant difference between the results of the tests performed existed. However, if the data was not normally distributed and homogeneous, the data would be analyzed using non-parametric statistics by means of the Kruskall Wallis method and, subsequently, a Post Hoc Mann Whitney U test. If the *P* value < 0.05; then a significant difference existed.

**Ethical conduct of research statement.** The animal study procedures were performed in accordance with the ethical clearance issued by The Ethics Commission of Faculty of Veterinary Medicine, Universitas Airlangga (Certificate number 2.KE.016.02.2020 dated February 4, 2020).

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## Author contributions

Q.A.: (1) conception and design of the work, data acquisition, data analysis and interpretation; (2) Drafting the article; (3) Final approval of the version to be published; (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. She wrote raw draft of manuscript and figures. A.M.: (1) conception and design of the work, data acquisition, data analysis and interpretation; (2) critically revising the article for important intellectual content; (3) Final approval of the version to be published; (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. He prepared the figures and edited the manuscript to be qualified for publishing. W.S.: (1) data analysis and interpretation; (2) critically revising the article for important intellectual content; (3) Final approval of the version to be published; (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. She gave and contributed for procedures of in vivo study for antiaging therapy. T.E.: (1) data analysis and interpretation; (2) Final approval of the version to be published; (3) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. She provided materials for the study and gave procedures for in vivo study for antiaging therapy. J.S.: (1) data analysis and interpretation; (2) Final approval of the version to be published; (3) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. He assessed the in vivo analysis for skin irritation. D.L.: (1) data analysis and interpretation; (2) Final approval of the version to be published; (3) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. He assessed the in vivo analysis for collagen density and number of fibroblast. All authors reviewed the manuscript.

## Competing interests

The authors declare no competing interests.

## Additional information

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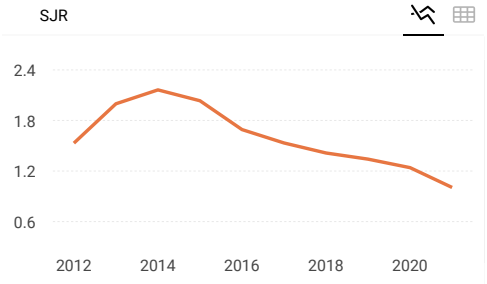


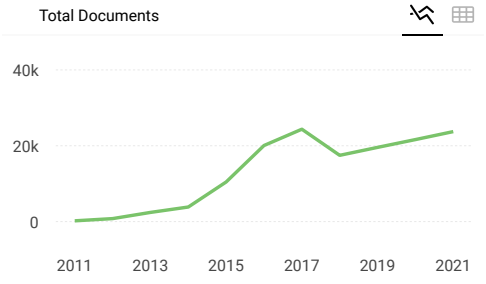


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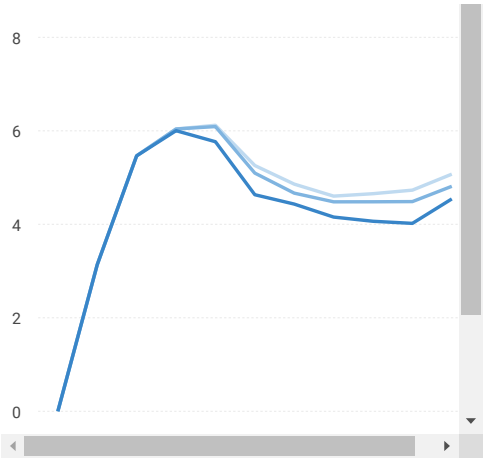


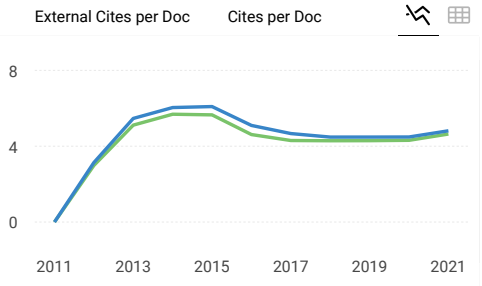


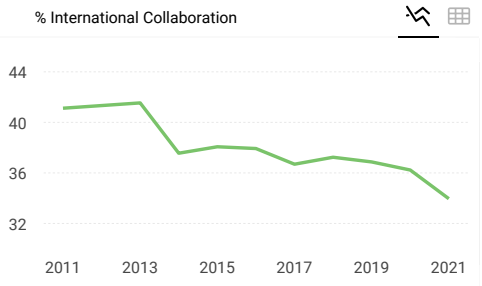


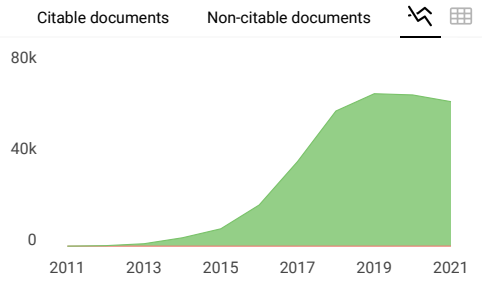


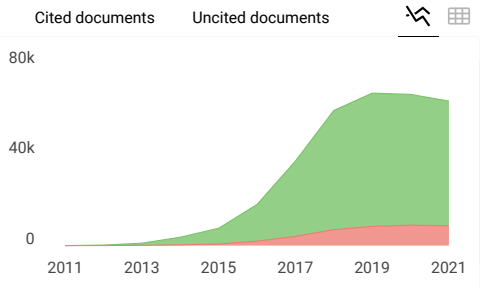


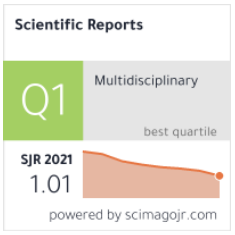


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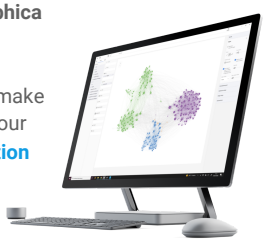



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