



**Journal of International Dental and Medical Research**



## **Journal of International Dental and Medical Research**

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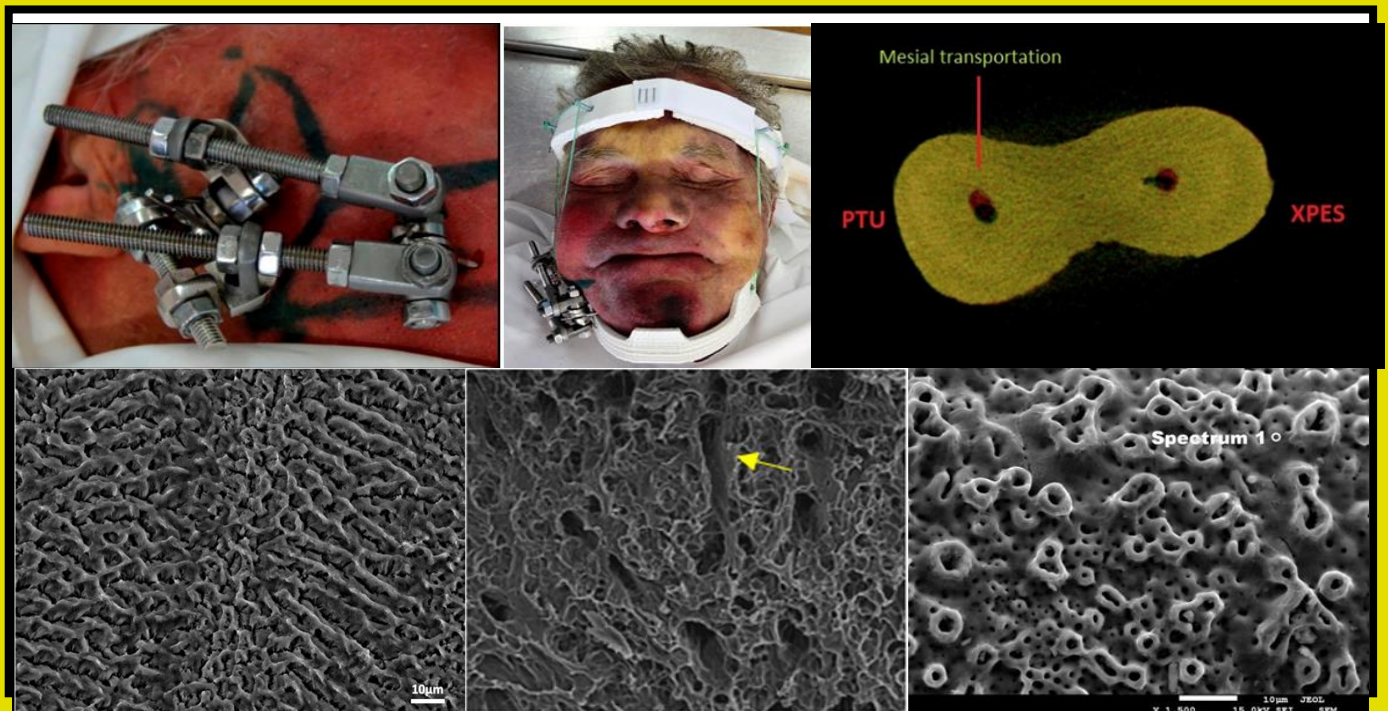


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2020 - Vol. 13 – No. 2

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DENTISTRY

## EXPERIMENTAL ARTICLE

1. **Mandible Exoskeleton - First Results of Development and Implementation**  
Alexandr A. Vorobyev, Denis Yu. Dyachenko, Yuliya A. Makedonova, Dmitriy V. Mikhailchenko,  
Evgeniy V. Fomichev, Karen A. Sargsyan  
Pages 400-406
2. **Evaluation of the Shaping Ability of XP Endo Shaper: A Micro-Computed Tomography Study**  
Sarah Mubarak Alkahtany, Sara Suliman Alrumaih, Mona Abdullah Alhassan, Basmah Ahmad Alnashmi,  
Ebtissam M. Al-Madi  
Pages 407-411
3. **Viability Test of Fish Scales Collagen from Oshphronemus Gouramy on Osteoblast Cell Culture**  
Agung Krismariono, Novia Wiyono, Chiquita Prah santi  
Pages 412-416
4. **Isolation and Antimicrobial Activity of Lactic Acid Bacteria against Streptococcus Mutans**  
Nor Zaihana Abdul Rahman, Rohazila Mohamad Hanafiah, Siti Aisyah Abd Ghafar, Norafiqah Abdullah,  
Nur Nabilah Azman  
Pages 417-421
5. **Clinical Control of Denture Base Acrylics Polymerization for the Quality Assurance: Pilot Study of Spectroscopic Approach**  
Yuriy Lokota, Ivan Paliichuk, Volodymyr Paliichuk, Myroslav Goncharuk-Khomyn  
Pages 422-429
6. **The Mangiferin (Mangifera Indica Linn) Effect Against the Calcium Degradation, Bones Resorption and Ossification of Rattus novergicus of Post-orthodontic treatment**  
Yenita Alamsyah, Nazruddin, Syafruddin Ilyas, Deddi Prima Putra  
Pages 430-435
7. **The Effect of Cranberry, Strawberry and Blueberry Juices on the Viability of Cariogenic Bacteria: An in Vitro Study**  
Md. Sofiqul Islam, Zainab Riaz, Anam Waqar, Mohannad Nassar, Ashfaque Hossain,  
Muhammed Mustahsen Rahman  
Pages 436-441
8. **Effects of Different Aging Methods on Color Change of Bulk-Fill and Anterior Resin Composites**  
**Effects of Aging Methods on Color Change of Composites**  
Makbule Tugba Tuncdemir, Kubra T. Kahraman  
Pages 442-447
9. **Efficiency of Cleaning the Various Types of Dental Implants' Surfaces (Tiu-Nite, Sla, Rbm) Using the Air-Flow Erythritol Method**  
Furtsev T.V., Zeer G.M.  
Pages 448-452
10. **Effect of Eucalyptus and Chloroform on Mineral Content of Radicular Dentin: an in vitro Study**  
Nexhmije Ajeti, Violeta Vula, Miranda Stavileci, Merita Barani, Agran Halimi, Lindihana Emiri  
Pages 453-458

- EXPERIMENTAL ARTICLE
- 11. Time Consumptions by Four Polishing Methods for in Vitro Removals of Orthodontic Adhesive Remnants**  
Kiatanan Sugsompian, Thosapol Piyapattamin  
Pages 459-462
- EXPERIMENTAL ARTICLE
- 12. The Microarchitecture and Atomic Mineral Composition of the Rats' Mandibular Condyle Varying Masticatory Functional Loads**  
Nur Masita Silviana, Sri Andarini, Diana Lyrawati, Mohammad Hidayat  
Pages 463-468
- EXPERIMENTAL ARTICLE
- 13. Scanning Electron Microscopic Evaluation for the Ability of Endovac and EnoActivator in Cleaning Root Canal Space Using EDTA and QMix™**  
Manal M. Abdelhafeez  
Pages 469-474
- EXPERIMENTAL ARTICLE
- 14. Radioprotective Effect of Spirulina Platensis on Head and Neck Radiation-Induced Xerostomia**  
Sarianoferni, Dian Mulawarmanti, Indeswati Diyatri, Eha Renwi Astuti, Soetjipto  
Pages 475-479
- EXPERIMENTAL ARTICLE
- 15. In vitro Analysis of Minimal Inhibitory Concentrations of NaOCl, CHX, MTAD, and EDTA against Enterococcus faecalis**  
Donika Bajrami, Miranda Stavileci, Agime Dragidella, Blerim Kamberi, Nora Aliu  
Pages 480-485
- EXPERIMENTAL ARTICLE
- 16. Influence of Root Canal Preparation with Different Tapers on Apical Leakage**  
Remy Barazy, George Eshoa  
Pages 486-490
- EXPERIMENTAL ARTICLE
- 17. RT-qPCR Gene Expression Analysis on the Irf6 Intron Polymorphism in Oral Epithelium of Non-Syndromic Oral Cleft Risk of Deutero-Malay Sub-Race Indonesian**  
Saskia L. Nasroen, Ani Melani Maskoen, Hardisiswo Soedjana, Dany Hilmanto  
Pages 491-496
- EXPERIMENTAL ARTICLE
- 18. Anti-Inflammatory Effect of Okra (*Abelmoschus esculentus*) Fruit Extract during Wound Healing Process after Tooth Extraction of Diabetic Wistar Rat**  
Muhammad Luthfi, Tuti Kusumaningsih, Agung Sosiawan, Hasna Shabrina  
Pages 497-502
- EXPERIMENTAL ARTICLE
- 19. Expression of Non-Metastatic Protein-23 And Metastatic Associated Protein-1 as a Molecular Target Therapy of an Oral Malignant Burkitt's Lymphoma Induced by Oligonucleotide P27 Sense**  
Supriatno, Ana Medawati, Sartari Entin Yuletnawati  
Pages 503-507
- EXPERIMENTAL ARTICLE
- 20. Enhancement of Osteogenesis Using a Combination of Hydroxyapatite and Stem Cells from Exfoliated Deciduous Teeth**  
Chiquita Prahasanti, Agung Krismariono, Rifiana Takanamita, I Komang Evan Wijaksana, Ketut Suardita, Tania Saskianti, Diah Savitri Ernawati  
Pages 508-512



## EXPERIMENTAL ARTICLE

**21. Pulpitis Induced Carotid Atherosclerosis**

Nadie Fatimatuazzahro, Rendra Chriestedy, IDA Susilawati, Wulandari Fajrin  
Pages 513-518

## EXPERIMENTAL ARTICLE

**22. Potency of Okra Fruit Extract (*Abelmoschus esculentus*) Against *Porphyromonas Gingivalis* as the Cause of Chronic Periodontitis**

Yuliati, Muhammad Luthfi, Priyawan Rachmadi, Bella Primordio Cida, Elvina Hasna Wijayanti  
Pages 519-524

## EXPERIMENTAL ARTICLE

**23. Combination of Anadara Granosa Shell-Stichopus Hermanni Gel on Osteoblast-Osteoclast and Blood Vessels in Femur Healing**

Rima Parwati Sari, Isnainy Nurlaily, Rizky Putri Heryana, Wahyu Fatmawati, Meinur Nur Ashrin  
Pages 525-532

## EXPERIMENTAL ARTICLE

**24. Enamel Remineralization Effect using Dewaxed Shellac Varnishes with Added Carbonate Apatite and Tricalcium Phosphate**

Arief Cahyanto, Dena Fadhillah Marwa, Kesya Saragih, Veni Takarini, Zulia Hasratiningsih  
Pages 533-538

## EXPERIMENTAL ARTICLE

**25. The Inhibitory Effect of Kaffir Lime Extract towards *Staphylococcus Aureus* Bacteria**

Sartika Puspita, Ovin Lutfialifta P  
Pages 539-542

## EXPERIMENTAL ARTICLE

**26. Effectivity of Insulin Leaf Extract (*Tithonia Diversivolia*) on Mice Malondialdehyde (MDA) Levels**

Tuti Kusumaningsih, Mohammed Aljunaid, Abdul Hafid Fauzi Barmen, Tantiana, Retno Palupi, Yuliati  
Pages 543-546

## EXPERIMENTAL ARTICLE

**27. The Expressions of Some Growth Factors as the Progressive Indicators of Pulmonary Arterial Hypertension**

Mahrus A. Rahman, I Ketut Alit Utamayasa, Agus Sunandar  
Pages 547-552

## EXPERIMENTAL ARTICLE

**28. Corticosteroid Effects and Administration Time Difference on Mice Model of Biliary Atresia**

Bagus Setyoboedi, Anang Endaryanto, Sjamsul Arief  
Pages 553-560

## CLINICAL ARTICLE

**29. The Role of Prooxidant-Antioxidant System in the Development of Alveolitis after Teeth Extraction**

Hutor N.S., Pidruchna S.R., Melnyk N.A., Avdeev O.V., Boykiv A.B., Kovtun N.Ya., Skochylo O.V., Tverdokhlib N.O., Goncharuk-Khomyn M.Y.  
Pages 561-565

## CLINICAL ARTICLE

**30. The Infraorbital Ethmoid (Haller's) Cells in a Group of Thai Patients: Panoramic Radiographic Study**

Chutamas Deepho, Sirilawan Tohnak, Ruchadaporn Kaomongkolgit, Ronnayut Chansamat, Weeraya Tantanapornkul  
Pages 566-570

## CLINICAL ARTICLE

- 31. Comparative Evaluation of Treatment Efficiency of Inflammatory Complications after Orthopedic Treatment with Up-To-Date Methods of Pharmacotherapy**  
Yuliya A. Makedonova, Dmitriy V. Mikhachenko, Alexandr V. Zhidovinov, Denis Yu. Dyachenko, Sergej A. Veremeenko  
Pages 571-576
- 32. Stress-Related Oral Manifestations Disorders in A Population Sample of Patients Attending Ajman University Dental Clinics**  
Ebtesam Khalil, Nihal A.Ibrahim, Maher Al Shayeb, Syed Kuduruthullah, Mawada Hassan  
Pages 577-586
- 33. Prevalence and Periodontal Treatment Needs of Aggressive Periodontitis, in Students of Specific part of Iran**  
Hossein Assarzadeh, Zahra Baghani, Rahil Mahmoodi  
Pages 587-594
- 34. Retrospective Study of the Prevalence of Type 2 Diabetes Mellitus and Severity of Periodontal Disease in Chronic Periodontitis Patients**  
Waleed Ahmed Ismail, Siti Lailatul Akmar Zainuddin, Romaisa Arshad Khokhar, Haslina Taib, Basaruddin Ahmad, Azlina Ahmad  
Pages 595-600
- 35. Social and Clinical Risk Determinants of Oral Lichen Planus – a Case Control Study**  
Jolanta Aleksejuniene, Arunas Rimkevicius, Alina Puriene, Ruta Rasteniene  
Pages 601-607
- 36. Relationship between the Nasopharyngeal Width and Hyoid Bone Position in Skeletal Malocclusion**  
Hilda Fitria Lubis, Lydia Irani Nainggolan, Alfrina Marwan  
Pages 608-613
- 37. Relapse in Modified Vacuum-Formed and Hawley Retainers for Transverse Expansion A Multicenter Randomized Control Trial**  
Lew Xian, Asma Ashari, Alizae Marny Fadzlin Syed Mohamed, Rohaya Megat Abdul Wahab, Elavarasi a/p Kuppusamy, Malathi Deva Tata, Yeoh Chiew Kit, Sindhu Sinnasamy  
Pages 614-621
- 38. Evaluation of Masticatory Efficiency among subjects with Removable Partial Dentures: A Comparative Study**  
Linda J Dula, Kujtim Sh. Shala, Arlinda Tmava-Dragusha, Zana Lila-Krasniqi, Teuta Pustina-Krasniqi, Teuta Bicaj  
Pages 622-627
- 39. Depression, Anxiety and Stress Among Pharmacy Students in Malaysia**  
Ali Sabri Radeef, Ghasak Ghazi Faisal  
Pages 628-632

- CLINICAL ARTICLE
- 40. Increased Hsp-72 Expression in Oral Mucormycosis after treatment with Hyperbaric Oxygen (HBO)**  
Fanny Margaretha Laihada, I Ketut Sudiana, M. Guritno S, Sumarno, Sunarjo, Retno Indrawati, Theresia Indah Budhy, Herjunianto, Titut Harnanik, Noengki Prameswari, Arya Brahmanta, Eddy Hermanto  
Pages 633-638
- CLINICAL ARTICLE
- 41. Miswak (Salvadora Persica) As an Alternative Oral Aid to Reduce Denture Induce Stomatitis on Edentulous Patients**  
Nusima Mohamed, Norlela Yacob, Wan Nor Syariza Wan Ali, Aida Ali, Nor Azlina Ismail, Nasadila Nadhira Nasser  
Pages 639-645
- CLINICAL ARTICLE
- 42. Diagnostic Value of Panoramic Radiography in Completely Edentulous Patients**  
Amaweya Abdulrahman Al-Sammarraie, Ayyam Khalid Abdulkareem  
Pages 646-650
- CLINICAL ARTICLE
- 43. Electromyography Activity of the Chewing Muscles During Adaptation among Complete Denture Wearers**  
Kujtim Sh. Shala, Linda J Dula, Venera Bimbashi  
Pages 651-658
- CLINICAL ARTICLE
- 44. Increasing Salivary Flow Rate and Salivary Ph after Consuming Secang Drink (Caesalpinia Sappan L.) Related to Body Mass Index**  
Winy Yohana, Sri Tjahajawati, Irna Sufiawati, Intan Safitri Kartika, Muhammad Iqbal Izdaulfikri  
Pages 659-662
- CLINICAL ARTICLE
- 45. Serum nitric oxide levels in smokers with chronic periodontitis**  
Hytham N Fageeh, Wael I Ibraheem, Abdullah A Meshni, Reghunathan S Preethanath  
Pages 663-668
- CLINICAL ARTICLE
- 46. The Relationship between Sex and Age on Dental Arch Change after Treatment with the Reverse Pull Face Mask Appliance of Class III Malocclusion: a Randomized Clinical Trial**  
Osama Bahaa Albajalan, Nawres Oraibi Alazzawi, Nor Ashikeen Mukti, A. R. Samsudin  
Pages 669-673
- CLINICAL ARTICLE
- 47. Sports-Related Dental Injury from the Perspective of Malaysian Athletes**  
Aiemeeza Rajali, Nik Rahayyu Nik Zulkifeli, Ahmad Safwan Mohd Elias, Nur Al Huda Mansur, Nik Haziman Wan Hamat, Syamsul Rizal Abu Amin  
Pages 674-681
- CLINICAL ARTICLE
- 48. Influence of Smoking upon the Ki67 Expressions in Asymptomatic Fully Impacted Lower Third Molar Follicles**  
Mhd Amer Alassfar, Mumdouh Almohareb, Haytham Bahhah  
Pages 682-688
- CLINICAL ARTICLE
- 49. Teeth and Soft Tissue Injuries as Well as Wound Healing Quality Patterns Among Primary School Students of Prishtina Region**  
Naim Haliti, Ragip Shabani, Shefqet Mrasori, Fatmir Dragidella, Hrvoje Juric, Nora Shabani Behrami, Dafina Doberdoli, Fehim Haliti  
Pages 689-696

- CLINICAL ARTICLE
- 50. The Practice, Perception, and Awareness of Self-Medication for Dental Pain in Malaysian Dental Students**  
Mahyunah Masud, Zaty Ainaa Mohamed, Nur Farhaanah Azman, Mohd Aizat Abdul Rahim  
Pages 697-703
- CLINICAL ARTICLE
- 51. The Comparison between Acetaminophen and Ibuprofen Effectiveness for Ductus Arteriosus Closure Therapy in Premature Infants**  
Mahrus A. Rahman, I Ketut Alit Utamayasa, Agus Cahyono  
Pages 704-707
- CLINICAL ARTICLE
- 52. Effectiveness of Treatment with Reverse Twin-Block and Reverse Pull Face Mask on Dental Arches of Class III Malocclusion: A Randomized Clinical Trial**  
Osama Bahaa Albajalan, Nawres Oraibi Alazzawi, Nor Ashikeen Mukti, A.R. Samsudin  
Pages 708-713
- CLINICAL ARTICLE
- 53. Characteristics of Dental Health, Dentomaxillar Growth and Body Mass Index in 3-6 years old Children in Yahya Kindergarten Bandung**  
Winnie Yohana, Rosiliwati Wihardja  
Pages 714-718
- CASE REPORT
- 54. Dilemma of Orthodontic Treatment in Fluorosed / Hypomineralised Enamel Teeth: A Case Report**  
Noor Ayuni Ahmad Shafiai, Alizae Marny Mohamed  
Pages 719-726
- CASE REPORT
- 55. Neutral Zone Impression Technique in Atrophic Mandibular Ridge using a Modified Design of Lower Base Plate**  
Ayman Al Oulabi, Zuryati Ab-Ghani, Noor Huda Ismail, Nafij Jamayet  
Pages 727-730
- REVIEW
- 56. The Advantage and Basic Approach of Infrared Thermography in Dentistry**  
Abdillah Imron Nasution, Mikhail Nikolaevich Pankov  
Pages 731-737
- REVIEW
- 57. Intrinsic Dental Erosion: Review of Dental Management**  
Mohammed Sulaiman Alruthea  
Pages 738-744
- REVIEW
- 58. Patient Satisfaction Measuring Instrument—A Scoping Review**  
Krisnawati Erry Tarman, Diah Ayu Maharani, Miesje K. Purwanegara  
Pages 745-751
- REVIEW
- 59. Recent Updates of the Oral Benefits of Mangosteen Plant Extracts: Review**  
Mohammed Aljunaid, Ninuk Hariyani, Retno Indrawati Roestamadji, Rini Devijanti Ridwan, Tuti Kusumaningsih, Huda Rashad Qaid  
Pages 752-757

**MEDICINE**

- EXPERIMENTAL ARTICLE**
- 60. The Effect of the Neurotransmitter Dopamine, Lead Acetate, L-NAME, and Verapamil on the Metabolic Pathway in the Longitudinal Smooth Muscle**  
Rahman Ferizi, Nora Shabani, Ragip Shabani, Naim Haliti  
Pages 758-768
- EXPERIMENTAL ARTICLE**
- 61. In Vitro Assay of Cornea Artificial Properties**  
Prihartini Widiyanti, Reni Prastyani  
Pages 769-773
- EXPERIMENTAL ARTICLE**
- 62. Smoke Effects of Disturbances Folliculogenesis (Mda, Gnrh, Hsp70, Apoptosis, and Follicles) in Ovarian on Mice Balb / C**  
Eny Susanti, I Ketut Sudiana, Hendy Hendarto  
Pages 774-777
- EXPERIMENTAL ARTICLE**
- 63. Lung Dendritic Cells Express Higher Stress Proteins on Higher Allergen Dose Exposure and Contribute to Allergen Tolerance Induction**  
Gatot Soegiarto, Agustina Tri Endharti, Wibi Riawan, Anang Endaryanto, Subijanto Marto Sudarmo  
Pages 778-784
- EXPERIMENTAL ARTICLE**
- 64. The Increasing Inflammatory Cells, Degeneration and Duodenal Necrosis on Infant Mice from Carbofuran Exposed Mothers**  
E. Z. Yanti, H. A. Hermadi, P. S. Rejeki, Y. Dhamayanti, Widjiati, E. M. Luqman  
Pages 785-790
- CLINICAL ARTICLE**
- 65. The Effect of Serum and Follicular Fluid Vitamin D on Intracytoplasmic Sperm Injection Outcome**  
Israa Majeed, Mohammad Oda Selman, Ban J. Qasim, Ghasak Ghazi faisal  
Pages 791-795
- CLINICAL ARTICLE**
- 66. Predictors of Time Delay in Commencing Primary Coronary Intervention in STEMI Kosova Case-Pilot Study**  
Hajdin Çitaku, Ramë Miftari, Fatmir Ferati, Xhevdet Krasniqi  
Pages 796-800
- CLINICAL ARTICLE**
- 67. Profile of Predictive Factors of Response to Therapy in Patients with Diffuse Large B-cell Lymphoma in dr Soetomo General Teaching Hospital Surabaya**  
Mochammad Dilliawan, Siprianus Ugroseno Yudho Bintoro, Putu Niken Ayu Amrita  
Pages 801-807
- CLINICAL ARTICLE**
- 68. Evaluating the Treatment of Patients with Appendicitis, Perspectives on Challenges Professional Work**  
Kadir Hysein, Valon Morina, Zeqir Hashani, Qenan Maxhuni, Rahman Ferizi  
Pages 808-815
- CLINICAL ARTICLE**
- 69. Comparison Study between Angio CT and USG Doppler for Early Detection of Arterial Stenosis of Lower Extremities in University Clinical Center of Kosovo**  
Lavdim H. Ymeri, Vjosa A. Zejnullahu, Serbeze Kabashi Muqaj, Muharrem Sadiku, Valon A. Zejnullahu  
Pages 816-823

**70. Curcumin as Adjuvant Therapy in COVID-19: Friend or Foe?**

Jeanne Adiwinata Pawitan

Pages 824-829

## Lung Dendritic Cells Express Higher Stress Proteins on Higher Allergen Dose Exposure and Contribute to Allergen Tolerance Induction

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### Abstract

Different doses of allergen lead to different T lymphocyte responses which partly explain the phenomenon of low or high dose tolerance. Dendritic cells (DC) are responsible for driving the T lymphocyte responses to a variety of exogenous stimuli, but the mechanisms are not completely understood.

Elucidate the mechanisms of how DCs drive the differentiation of T lymphocytes in response to different doses of allergen.

Groups of male BALB/c mice (n=4-5) were sensitized intraperitoneally with sham or different doses (low: 10 µg, high: 1000 µg) of Der P1 (house dust mite allergen). They were exposed daily to aerosolized Der p1 allergen for 7 consecutive days. Different concentrations of Der p1 solution were nebulized: sham, low dose (15 µg/mL), or high dose (1500 µg/mL). Bronchoalveolar lavage fluid (BALF) was obtained from the lungs. Levels of IL-12 in BALF were measured. Lung tissue sections were then stained to detect the expression of Hsp70 by lung DCs.

Lung DCs exposed to a higher sensitizing doses of Der p1 allergen tend to express significantly higher levels of Hsp70 and secrete higher levels of IL-12 in BALF. There was a significant positive correlation between the levels of Hsp70 expression by lung DCs with IL-12 levels in BALF (r=0.581).

Higher exposure doses of allergen puts lung DCs under stressed condition thereby induced high expression of 'stress proteins' which may explain the mechanism of DCs drive the T lymphocyte response.

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### Introduction

Different exposure doses of allergen leads to different direction of T lymphocyte responses which partly explain the phenomenon of low or high dose tolerance<sup>1-3</sup>. Dendritic cells are cells that responsible for driving the appropriate T lymphocyte responses to a variety of exogenous stimuli<sup>4,5</sup>, but the mechanisms by

which they perform that task are not completely understood.

Other studies have shown that dendritic cells exposed to some stressful conditions from the environment (heat, ultraviolet radiation or heavy metals), pathological insults (infections or malignancies), or physiological stimuli (growth factors or cell differentiation) induce a marked increase in heat shock proteins (HSPs) synthesis, a phenomenon known as the stress response<sup>6-8</sup>.

These HSPs are shown to induce the production and release of a variety of pro-inflammatory cytokines, including IL-12, nitric oxide and C-C chemokines by monocyte, macrophage and dendritic cells. They also induce the maturation of dendritic cells which enable these cells to activate T lymphocytes as demonstrated by the up-regulation of MHC class

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I and II molecules, co-stimulatory molecules such as B7-1 and B7-2<sup>9-11</sup>. Recently, it has been shown that HSPs play an important role in antigen direct and cross-presentation because they can bind antigenic peptides generated within the cells, form HSP-peptide complexes. When released into extracellular compartment the HSP-peptide complexes can be recognized and taken up by other dendritic cells via CD91-mediated endocytosis, resulting in representation of the antigenic peptide by dendritic cells to T lymphocytes with the peptide specific receptor<sup>9,12,13</sup>.

Using cellular stress and homeostasis paradigm, it can be speculated that dendritic cells exposed to high dose of allergen are under stressful condition and thereby release or produce stress protein such as HSPs and certain cytokines. The present study aim to answer the following questions: can the mechanism by which dendritic cells drive the differentiation of T lymphocytes under different exposure doses of allergen be explained through the 'cellular stress concept', and are dendritic cells that exposed to high doses of allergen indeed under stress and thereby express or secrete high amount of 'stress proteins' which also act as 'danger signals' that used by dendritic cells to drive the differentiation of T lymphocytes?

## Materials and methods

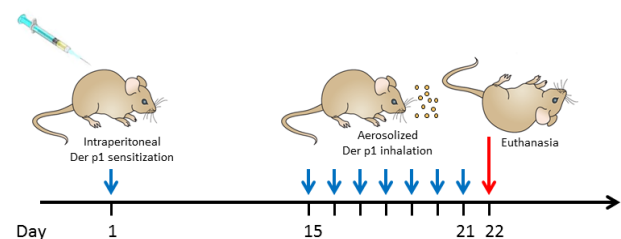
### Mice

Male inbred BALB/c mice of about 8-10 weeks old were purchased from Japan SLC, Inc. (Shizuoka, Japan) via PN Biofarma (Bandung, Indonesia). Food and water were provided ad libitum and mice were kept in a 12 h-light, 12 h-dark cycle in a specific pathogen free condition according to Federation of European Laboratory Animal Science Associations (FELASA) recommendation<sup>14</sup>. The local Ethical Committee (ACUC Veterinary Faculty Universitas Airlangga) approved the in vivo manipulations used in this study with certificate No. 150-KE.

### Sensitization and Allergen Challenge Protocol

Sensitization and challenge were performed according to the method by Tournoy et al<sup>15</sup> with some modifications. The lyophilized natural major house dust mite allergen (Der p1) was purchased from Greer Laboratories (Lenoir, N.C., USA). Groups of mice (n=4-5) were

sensitized intraperitoneally with sham (phosphate-buffered saline/PBS), or low dose (10 µg), or high dose (1000 µg) injection of major house dust mite allergen (Der p1) adsorbed to 20:1 ratio of aluminium hydroxide (Al(OH)<sub>3</sub>) solution (Pierce Biochemicals, Thermo Fisher Scientific (Hong Kong) Ltd, Shatin, Hong Kong). Fourteen days later, the mice were exposed daily to aerosolized Der p1 allergen for 7 consecutive days (days 15-21). The mice were individually placed in a 50-ml plastic tube and exposed to aerosolized Der p1 allergen for 30 min. The aerosol was produced by Pulmo-Aide E0570 compressor nebulizer (DeVilbiss Corp., Somerset, PA, USA), driven by compressed air at 5-9 L/min. Different concentrations (doses) of Der p1 solution were nebulized: sham (PBS), low dose (15 µg/mL), or high dose (1500 µg/mL) solutions. The illustration for the protocol can be seen in Figure 1.



**Figure 1.** The scheme of our study protocol: mice intraperitoneal sensitization, aerosol inhalation exposure, and euthanasia.

### Bronchoalveolar Lavage (BAL) and Measurement of IL-12

Mice were put under anesthesia at 24 h after the last challenge (day 22). BALF was obtained from the whole lungs by inserting a cannula into the surgically exposed trachea for cell analysis. BAL was performed via 3 intratracheal instillations with 0.3 ml Hank's balanced salt solution (HBSS) + 1% Bovine Serum Albumin (BSA), followed by 3 instillations with 1 ml of HBSS to collect cells for cytospin analysis as previously described<sup>15,16</sup>. The BAL fluid of the first three fractions was centrifuged and the supernatant was used for cytokine (IL-12) detection and measurement. IL-12 levels in BALF were measured using standard indirect ELISA method. After staining with May-Grünwald-Giemsa, total and differential cell counts were done using standard morphologic criteria.



### Preparation of Lung and Lymph nodes

Immediately after BAL, the mice were killed by right cardiac puncture and blood aspiration using an 18 gauge polyurethane catheter (Becton Dickinson, Madrid, Spain). The collected blood was used for measurement of serum cytokines. Pulmonary and systemic circulation were then perfused with saline/EDTA to remove the intravascular pool of cells. Paratracheal and parathymic intrathoracic lymph nodes were collected in steril petri dishes on ice for other studies. Lungs were carefully separated from thymic and cardiovascular remnants and removed in toto, including the main brochi and trachea. Left lung was separated for histological and immunohistochemical examination. Right lung was thoroughly minced using iridectomy scissors and incubated for 30 min in digestion medium in a humidified incubator at 37°C and 5% CO<sub>2</sub>, according to a modified protocol<sup>17</sup> and further used for other studies.

### Histological examination

For histological examination, the left lung was removed and fixed in 4% paraformaldehyde. Then, the tissues were embedded in resin (Jung HistoResin Plus; Reichert/Jung, Heidelberg, Germany) and cut into 2-µm sections, which were stained with hematoxylin and eosin (H-E).

### Measurement of Hsp70 expression by lung dendritic cells

For immunohistochemical analysis, some of the lung tissue sections were deparaffinized and underwent standard procedures for antigen retrieval<sup>18</sup>. Tissue sections were then double stained to detect the expression of Hsp70 by lung dendritic cells. Anti CD11c and anti-hsp70 monoclonal antibodies were used (Santa Cruz Biotechnology, Santa Cruz, CA, USA). CD11c positive dendritic cells were stained with 3,3'-diaminobenzidine (DAB), while Hsp70 were stained with light violet blue (LV blue). Methyl green was used as counterstaining. Tissue sections for this process were mounted using 5% gelatin. Examination and interpretation of Hsp70 expression by lung dendritic cells was done by two independent observers. Expression scoring was done according to modification of the method of Soini et al<sup>19</sup> and Pizem et al<sup>20</sup>. Scores from both observers were checked for consistency.

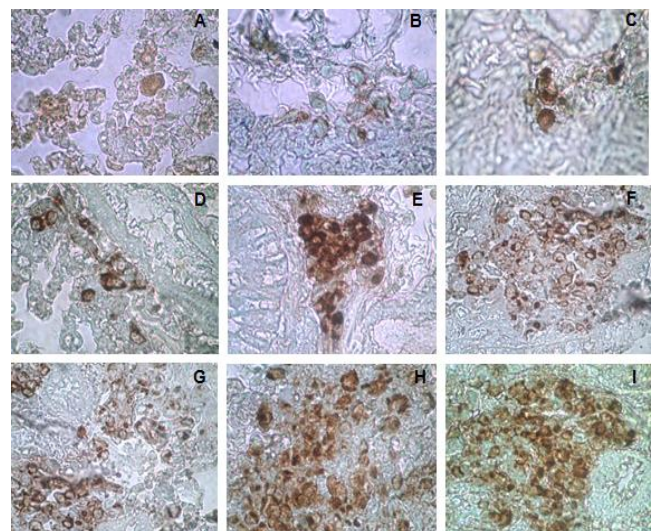
### Statistical Analysis

Data were analyzed with the statistical package SPSS 16.0 (SPSS Inc., Chicago, IL). Values are expressed as mean ± SD. To check the consistency of Hsp70 expression scoring by two independent observers paired t test and Pearson's correlation were used. Kolmogorov-Smirnov test was used to check the normality of data distribution, and Levine's test was used to check the homogeneity of data variant. The differences between the groups were tested using ANOVA. For data with abnormal distribution Kruskal-Wallis A and Kendall Tau analysis were used. Pearson's test was used to determine correlation between Hsp70 expression scores and IL-12 levels. P <0.05 was accepted as statistically significant.

### Results

#### Lung Dendritic Cells Exposed to High Sensitizing and Inhalation Doses of Der p1 Allergen Express High Levels of Hsp70

The expression of Hsp70 in lung dendritic cells under different sensitizing and inhalation doses of Der p1 allergen is shown in Figure 2.

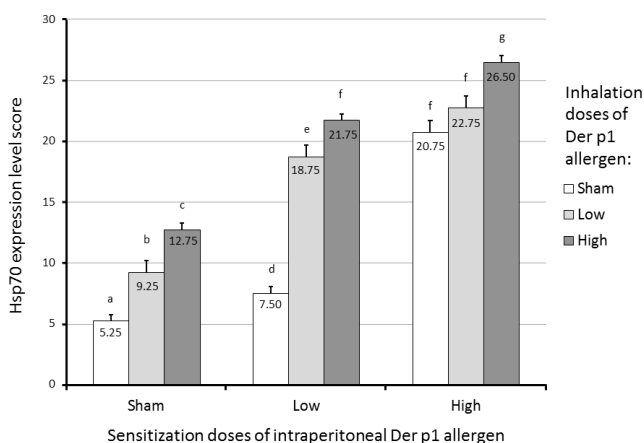


**Figure 2.** The representative expressions of heat shock protein Hsp70 by lung dendritic cells under different sensitizing and inhalation dose of Der p1 allergen.

The above figures shows the representative expressions of heat shock protein 70 (Hsp70) by lung dendritic cells in groups of mice (n=4-5) exposed to different sensitizing and inhalation

dose of Der p1 allergen as seen under light microscopy (1000x magnification) in immunohistochemistry (IHC) lung tissue sections. We use double staining technique to reveal lung dendritic cells (CD11c positive) which express Hsp70 (Hsp70 positive). (A: control mice, B: sham sensitization + low dose inhalation, C: sham sensitization + high dose inhalation, D: low dose sensitization + sham inhalation, E: low dose sensitization + low dose inhalation, F: low dose sensitization + high dose inhalation, G: high dose sensitization + sham inhalation, H: high dose sensitization + low dose inhalation, I: high dose sensitization + high dose inhalation).

Interpretation and scoring were done by two independent observers, both showed high consistency ( $t=1.922$ ,  $p=0.063$ ;  $r=0.974$ ,  $p\leq 0.001$ ). The relative expression scores for each group of interventions were measured and shown in Figure 3.



**Figure 3.** Relative Hsp70 expression by lung dendritic cells under different sensitizing and inhalation dose of Der p1 allergen.

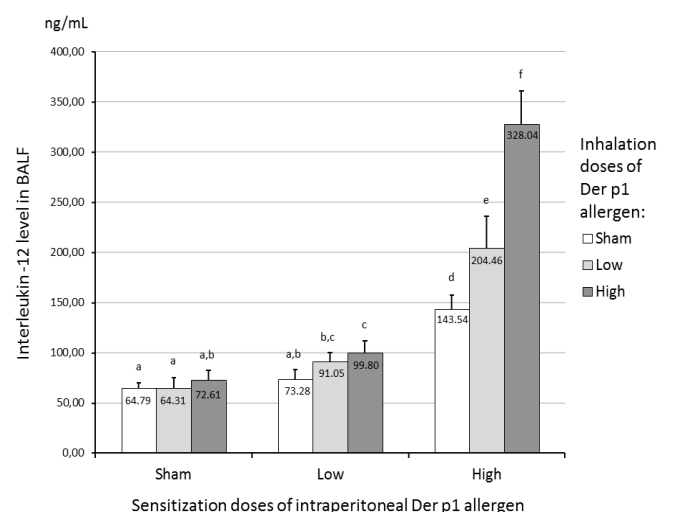
Mean values of relative heat shock protein 70 (Hsp70) expression in each group of mice ( $n=4-5$ ) and the respective standard error bars were presented. Groups marked with different alphabet (a,b,c,d,e,f, and g) showed significantly different expression score ( $p<0.05$ ). Groups with the same alphabetical marks had non-significant difference in Hsp70 expression.

Lung dendritic cells that were exposed to a higher intraperitoneal sensitizing doses of Der p1 allergen tend to express significantly higher levels of Hsp70 (Figure 3). This tendency was

also seen if we modulate the inhalation dose of Der p1 allergen (low dose inhalation, grey bars, and high dose inhalation, dark grey bars). Coupling effects were seen, as the higher the sensitizing doses and the higher the inhalation doses, the higher the expressions of Hsp70. The non-significant difference of Hsp70 expression between sham inhalation and low inhalation in groups with high sensitization dose (20.75 vs. 22.75 respectively,  $p>0.05$ ), indicates that the sensitizing dose is more important in determining the Hsp70 expression by lung dendritic cells than the inhalation dose.

### Higher Level of IL-12 was Detected in BALF in Group of Mice Exposed to Higher Sensitizing and Inhalation Doses of Der p1 Allergen

Similar to the expression levels of Hsp70 by lung dendritic cells, higher intraperitoneal sensitizing doses of Der p1 allergen tend to result in increased levels of IL-12 in BALF (Figure 4). The same tendency was also seen if we modulate the inhalation dose of Der p1 allergen (low dose inhalation, grey bars, and high dose inhalation, dark grey bars). Coupling effects were also seen, as the higher the sensitizing doses and the higher the inhalation doses, the higher the levels of IL-12 in BALF, particularly in groups which received high sensitization doses of intraperitoneal Der p1 allergen (143.54, 204.46, and 328.04 respectively,  $p<0.05$ ).

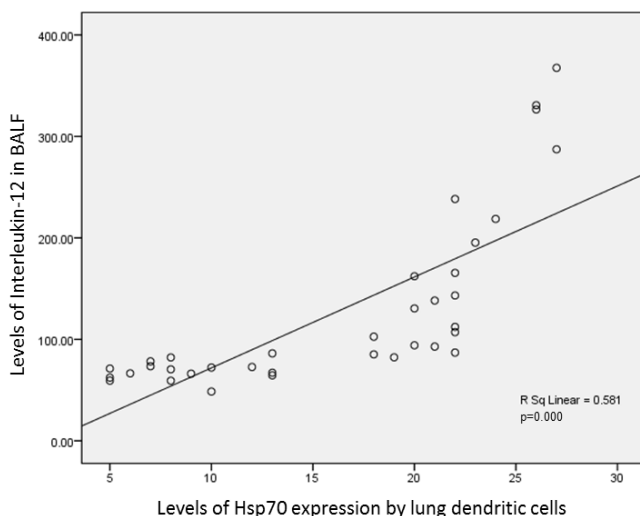


**Figure 4.** Interleukin-12 levels in bronchoalveolar lavage fluid under different sensitizing and inhalation dose of Der p1 allergen.

Mean values of interleukin-12 (IL-12) levels in each group of mice (n=4-5) and the respective standard error bars were presented. Groups marked with different alphabet (a,b,c,d,e, and f) showed significantly different IL-12 levels compared to other groups ( $p < 0.05$ ). Groups with the same alphabetical marks had non-significant difference in IL-12 levels.

### The expression levels of Hsp70 by lung dendritic cells significantly correlated with IL-12 levels in BALF

There was a significant positive correlation between the levels of Hsp70 expression by lung dendritic cells with IL-12 levels in BALF ( $r = 0.581$ ;  $p \leq 0.001$ ; Figure 5). This result implies that the stressed lung dendritic cells expressed high levels of stress protein which also associated with the levels of IL-12, which in turn contribute to the induction of Th1 type immune response or a shift from the initial Th2 type immune response.



**Figure 5.** Correlation between levels of Hsp70 expression by lung dendritic cells with interleukin-12 levels in bronchoalveolar lavage fluid (BALF).

The higher the heat shock protein 70 (Hsp70) expression levels by lung dendritic cells, the higher the IL-12 levels in BALF ( $r = 0.581$ ,  $p \leq 0.001$ ).

### Discussion

One of the mechanisms by which dendritic cells drive the differentiation of T lymphocytes

can be explained through the 'cellular stress concept'. As has been shown in the present study, dendritic cells that exposed to a high sensitization and inhalation dose of allergen (Der p1) are indeed under stress, as demonstrated by high level of 'stress protein' (Hsp70) expression compared to dendritic cells that exposed to 'usual' or low sensitization and inhalation dose.

'Cellular stress concept' stated that any cell exposed to a variety of environmental stressors, including extremes of temperature, ultraviolet radiation, toxins, or infections undergo some damage in the cellular component which interfere with cellular essential functions. In response to this, the 'stressed' cell utilize certain cellular stress response that serve as an adaptive purpose to protect itself from unfavourable environmental conditions, both through short term mechanisms that minimize acute damage to the cell's overall integrity, and through longer term mechanisms which provide the cell a measure of resiliency against similar adverse conditions. One of the mechanisms that has been extensively studied is the expression heat shock or heat stress proteins (HSPs)<sup>6</sup>. Traditionally, HSPs are regarded as intracellular molecules which only released into extracellular compartments upon necrotic cell death. However, recently it has been shown that HSPs can be actively released extracellularly in response to a number of stressful conditions<sup>20</sup>. Our study result showed that exposure to high dose of allergen can be viewed as one of the stressful conditions.

Functionally, stress-inducible proteins can be grouped into seven classes. The predominant class of HSPs, the molecular chaperones, comprises five major and broadly conserved families-Hsp100s, Hsp90s, Hsp70s, Hsp60s, and small HSPs<sup>6</sup>. One of the most highly conserved chaperones is the Hsp70 protein. Under physiological conditions, this protein are involved in the de novo folding of proteins, but during and following stressful conditions, Hsp70 functions as a chaperone which enable the cell to cope with harmful aggregations of denaturated proteins. Thus, its extracellular expression confers protection against stresses that induce protein damage<sup>21</sup>. These phenomenon were observed in cultured cells, animal models, and human tissues, resulting from various stressful stimuli<sup>22,23</sup>. The mechanisms of active HSP release are somewhat controversial because initially researchers cannot identify any signal peptide

that targets this protein for classical secretion. Recent findings suggest that HSP was released by a non-classical protein transport pathway that requires intact membrane lipid rafts for efficient release. Others also demonstrated that HSP were secreted within exosomes<sup>24-26</sup>.

One of the proposed functions of extracellular HSP is immune activity modulation. Many of these effects are mediated by cell surface receptors such as c-type lectin receptors and scavenger receptors expressed on a wide range of cell types<sup>27</sup>. Secreted Hsp70 were shown to induce significant cytokines release including IL-1 $\beta$ , TNF- $\alpha$ , and IL-12 by macrophages and dendritic cells<sup>28-30</sup>. Our study confirmed these findings and showed that lung dendritic cells exposed to a higher dose of Der p1 allergen not only express higher level of Hsp70 but also secrete higher level of IL-12. Our study found a significant positive correlation between the levels of Hsp70 expression by lung dendritic cells with IL-12 levels in BALF. It is of particular interest that other studies also observed a significant increase in Hsp70 (and thus, antibodies against Hsp70) in subjects who were exposed to environmental stresses such as carbon monoxide, heat, and dust<sup>31</sup>. Although not specifically mentioned in their report, we know that house dust mite like *Dermatophagoides pteronyssinus* is the dominant component of dust in the living environment<sup>32</sup>. Hsp70 was also reported to be present in the skin of allergic contact hypersensitivity model<sup>33</sup>, indicating that Hsp70 is also an important mediators of allergic inflammation. All of those findings, either directly or indirectly, supported our study results.

As stated previously, extracellular HSP had been reported to activate macrophages, and dendritic cells via a receptor-mediated process<sup>28,34</sup>. Activated and mature macrophages or dendritic cells then express some costimulatory signals that are needed for naïve T lymphocytes priming and activation<sup>35</sup>. In our study, the expression of Hsp70 and the secretion of IL-12 can be viewed as the third signals that drive T lymphocyte differentiation.

In conclusion, using our approach with differential sensitizing and inhalation doses of allergen, we elucidate one of the mechanisms by which dendritic cells sensing the 'danger' or the 'stressful condition' in the microenvironment, and make use the 'stress protein' they express or secrete to alert naïve T lymphocytes dan drive

their appropriate direction of differentiation and ultimately determine the immune response toward immune tolerance to allergen. With this 'cellular stress concept', we can prove that the more 'stressed' the dendritic cells, the more 'stress protein' they secrete, and.

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### Declaration of Interest

All of the authors declare that there are no potential conflicts of interest in relation to this manuscript writing and publication.

### References

1. Woodfolk JA. High-dose allergen exposure leads to tolerance. *Clinical reviews in allergy & immunology*. 2005;28(1):43-58.
2. Michallet M-C, Saltel F, Flacher M, Revillard J-P, Genestier L. Cathepsin-Dependent Apoptosis Triggered by Supraoptimal Activation of T Lymphocytes: A Possible Mechanism of High Dose Tolerance. *The Journal of Immunology*. 2004;172(9):5405-14.
3. Nurieva RI, Liu X, Dong C. Molecular mechanisms of T-cell tolerance. *Immunological reviews*. 2011;241(1):133-44.
4. Kadowaki N. Dendritic Cells—A Conductor of T Cell Differentiation—. *Allergology International*. 2007;56(3):193-9.
5. Diebold SS. Determination of T-cell fate by dendritic cells. *Immunology & Cell Biology*. 2008;86(5):389-97.
6. Richter K, Haslbeck M, Buchner J. The Heat Shock Response: Life on the Verge of Death. *Molecular Cell*. 2010;40(2):253-66.
7. Bakthisaran R, Tangirala R, Rao CM. Small heat shock proteins: Role in cellular functions and pathology. *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics*. 2015;1854(4):291-319.
8. Fulda S, Gorman AM, Hori O, Samali A. Cellular Stress Responses: Cell Survival and Cell Death. *International Journal of Cell Biology*. 2010;2010:23.
9. Basu S, Binder RJ, Suto R, Anderson KM, Srivastava PK. Necrotic but not apoptotic cell death releases heat shock proteins, which deliver a partial maturation signal to dendritic cells and activate the NF- $\kappa$ B pathway. *International immunology*. 2000;12(11):1539-46.
10. Panjwani NN, Popova L, Srivastava PK. Heat Shock Proteins gp96 and hsp70 Activate the Release of Nitric Oxide by APCs. *The Journal of Immunology*. 2002;168(6):2997-3003.
11. Wang Y, Kelly CG, Singh M, McGowan EG, Carrara A-S, Bergmeier LA, et al. Stimulation of Th1-Polarizing Cytokines, C-C Chemokines, Maturation of Dendritic Cells, and Adjuvant Function by the Peptide Binding Fragment of Heat Shock Protein 70. *The Journal of Immunology*. 2002;169(5):2422-9.

12. Li Z, Menoret A, Srivastava P. Roles of heat-shock proteins in antigen presentation and cross-presentation. *Current Opinion in Immunology*. 2002;14(1):45-51.
13. Murshid A, Gong J, Calderwood SK. The role of heat shock proteins in antigen cross presentation. *Frontiers in immunology*. 2012;3:63-.
14. Basu S, Binder RJ, Ramalingam T, Srivastava PK. CD91 Is a Common Receptor for Heat Shock Proteins gp96, hsp90, hsp70, and Calreticulin. *Immunity*. 2001;14(3):303-13.
15. Mähler M, Berard M, Feinstein R, Gallagher A, Illgen-Wilcke B, Pritchett-Corning K, et al. FELASA recommendations for the health monitoring of mouse, rat, hamster, guinea pig and rabbit colonies in breeding and experimental units. *Laboratory Animals*. 2014;48(3):178-92.
16. Tournoy, Kips, Schou, Pauwels. Airway eosinophilia is not a requirement for allergen-induced airway hyperresponsiveness. *Clinical & Experimental Allergy*. 2000;30(1):79-85.
17. Moerloose KB, Robays LJ, Maes T, Brusselle GG, Tournoy KG, Joos GF. Cigarette smoke exposure facilitates allergic sensitization in mice. *Respiratory research*. 2006;7(1):49-.
18. Hove CLV, Maes T, Joos GF, Tournoy KG. Prolonged Inhaled Allergen Exposure Can Induce Persistent Tolerance. *American Journal of Respiratory Cell and Molecular Biology*. 2007;36(5):573-84.
19. Misharin AV, Morales-Nebreda L, Mutlu GM, Budinger GRS, Perlman H. Flow cytometric analysis of macrophages and dendritic cell subsets in the mouse lung. *American journal of respiratory cell and molecular biology*. 2013;49(4):503-10.
20. D'Amico F, Skarmoutsou E, Stivala F. State of the art in antigen retrieval for immunohistochemistry. *Journal of Immunological Methods*. 2009;341(1):1-18.
21. Soini Y, Pääkkö P, Lehto VP. Histopathological evaluation of apoptosis in cancer. *The American journal of pathology*. 1998;153(4):1041-53.
22. Pizem J, Coer A. Detection of apoptotic cells in tumour paraffin sections. *Radiology and Oncology*. 2003;37(4):225-32.
23. Liao D-F, Jin Z-G, Baas AS, Daum G, Gygi SP, Aebersold R, et al. Purification and Identification of Secreted Oxidative Stress-induced Factors from Vascular Smooth Muscle Cells. *Journal of Biological Chemistry*. 2000;275(1):189-96.
24. Daugaard M, Rohde M, Jäättelä M. The heat shock protein 70 family: Highly homologous proteins with overlapping and distinct functions. *FEBS Letters*. 2007;581(19):3702-10.
25. Tang D, Khaleque MA, Jones EL, Theriault JR, Li C, Wong WH, et al. Expression of heat shock proteins and heat shock protein messenger ribonucleic acid in human prostate carcinoma in vitro and in tumors in vivo. *Cell stress & chaperones*. 2005;10(1):46-58.
26. Rajdev S, Hara K, Kokubo Y, Mestril R, Dillmann W, Weinstein PR, et al. Mice overexpressing rat heat shock protein 70 are protected against cerebral infarction. *Annals of Neurology*. 2000;47(6):782-91.
27. Bausero MA, Gastpar R, Multhoff G, Asea A. Alternative mechanism by which IFN-gamma enhances tumor recognition: active release of heat shock protein 72. *Journal of immunology* (Baltimore, Md : 1950). 2005;175(5):2900-12.
28. Lancaster GI, Febbraio MA. Exosome-dependent Trafficking of HSP70: A NOVEL SECRETORY PATHWAY FOR CELLULAR STRESS PROTEINS. *Journal of Biological Chemistry*. 2005;280(24):23349-55.
29. Vega VL, Rodríguez-Silva M, Frey T, Gehrmann M, Diaz JC, Steinem C, et al. Hsp70 Translocates into the Plasma Membrane after Stress and Is Released into the Extracellular Environment in a Membrane-Associated Form that Activates Macrophages. *The Journal of Immunology*. 2008;180(6):4299-307.
30. Murshid A, Theriault J, Gong J, Calderwood SK. Investigating receptors for extracellular heat shock proteins. *Methods in molecular biology* (Clifton, NJ). 2011;787:289-302.
31. Colaco CA, Bailey CR, Walker KB, Keeble J. Heat Shock Proteins: Stimulators of Innate and Acquired Immunity. *BioMed Research International*. 2013;2013:11.
32. Somensi N, Brum PO, de Miranda Ramos V, Gasparotto J, Zanotto-Filho A, Rostirolla DC, et al. Extracellular HSP70 Activates ERK1/2, NF-kB and Pro-Inflammatory Gene Transcription Through Binding with RAGE in A549 Human Lung Cancer Cells. *Cellular Physiology and Biochemistry*. 2017;42(6):2507-22.
33. Mansilla MJ, Costa C, Eixarch H, Tepavcevic V, Castillo M, Martin R, et al. Hsp70 Regulates Immune Response in Experimental Autoimmune Encephalomyelitis. *PLOS ONE*. 2014;9(8):e105737.
34. Wu T, Tanguay RM. Antibodies against heat shock proteins in environmental stresses and diseases: friend or foe? *Cell stress & chaperones*. 2006;11(1):1-12.
35. Kim J, Lee S, Woo S-y, Han Y, Lee JH, Lee I-Y, et al. The indoor level of house dust mite allergen is associated with severity of atopic dermatitis in children. *Journal of Korean medical science*. 2013;28(1):74-9.
36. Yusuf N, Nasti TH, Huang C-M, Huber BS, Jaleel T, Lin H-Y, et al. Heat shock proteins HSP27 and HSP70 are present in the skin and are important mediators of allergic contact hypersensitivity. *Journal of immunology* (Baltimore, Md : 1950). 2009;182(1):675-83.
37. Paltsev M, Severin S, Danilevskii M, Moskaleva EY. Regulation of the physiological functions of human dendritic cells by recombinant heat shock protein Hsp70. *Neuroscience and Behavioral Physiology*. 2011;41(1):74-82.
38. Sallusto F, Lanzavecchia A. The instructive role of dendritic cells on T-cell responses. *Arthritis research*. 2002;4 Suppl 3(Suppl 3):S127-S32.



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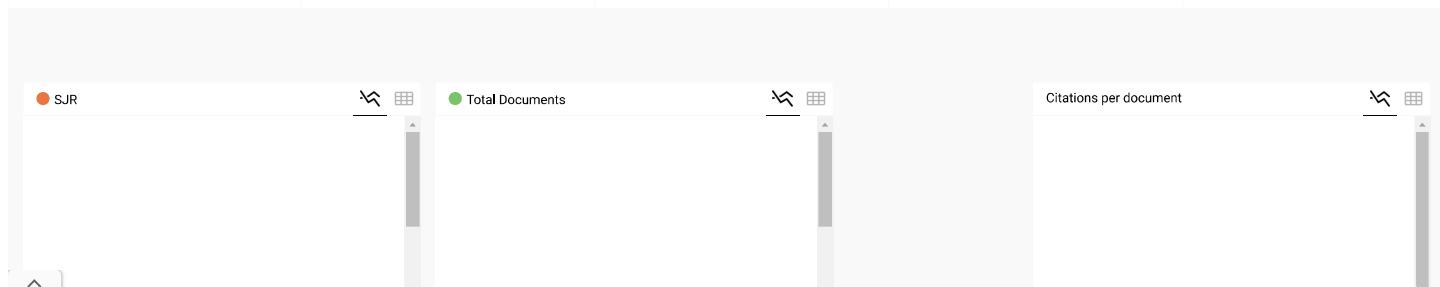
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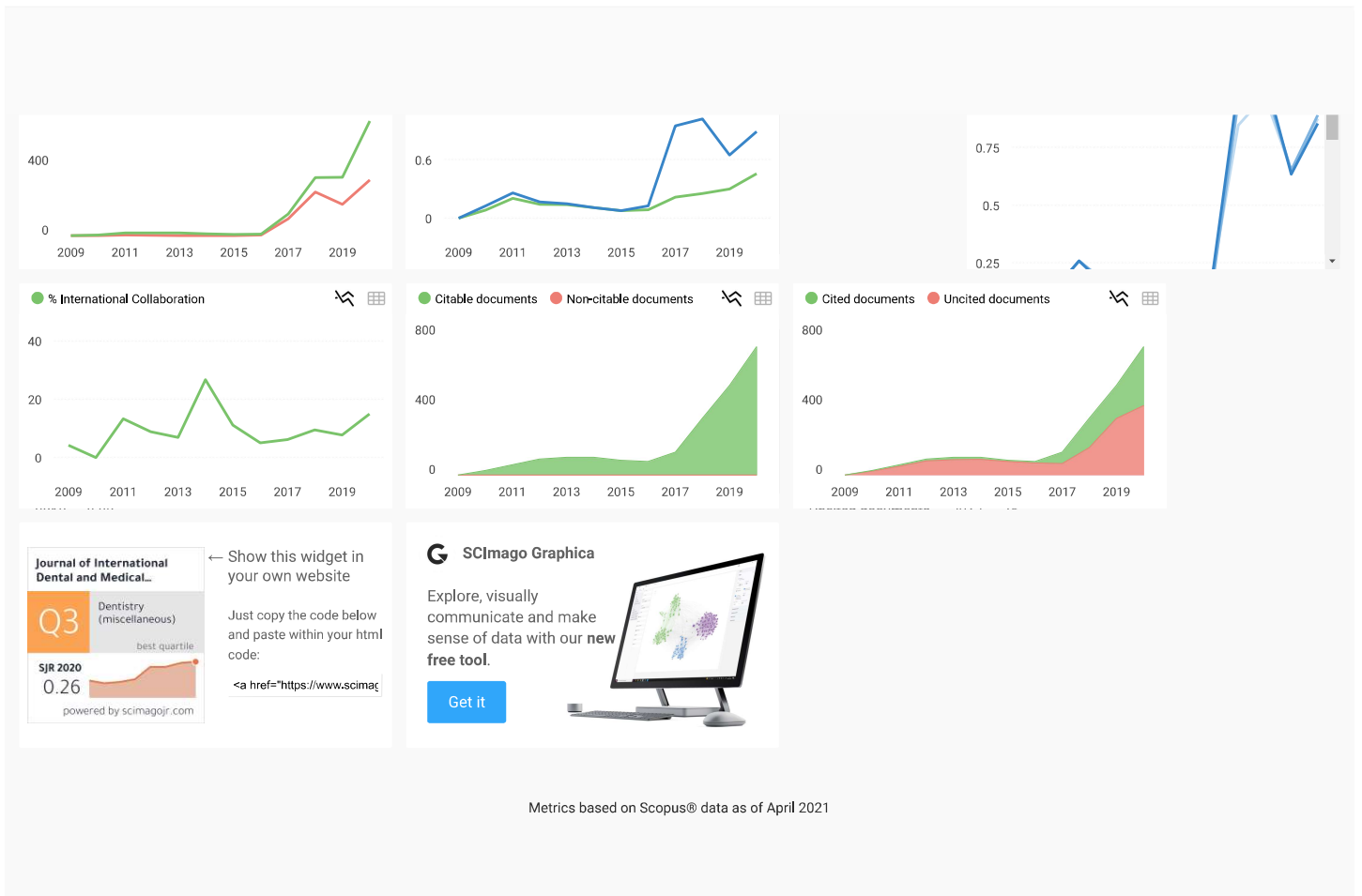
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