

DAFTAR ISI

	Halaman
Lembar Sampul Depan	
Lembar Sampul Dalam.....	i
Halaman Prasyarat Gelar.....	ii
Pernyataan Keaslian Penelitian.....	iii
Lembar Persetujuan.....	iv
Penetapan Panitia Penguji.....	v
Ucapan Terima Kasih.....	vi
Abstrak.....	x
<i>Abstract</i>	xi
DAFTAR ISI.....	xii
DAFTAR TABEL.....	xiv
DAFTAR GAMBAR.....	xv
DAFTAR SINGKATAN.....	xvi
BAB 1 PENDAHULUAN	
1.1 Latar Belakang.....	1
1.2 Rumusan Masalah.....	4
1.3 Tujuan Penelitian.....	4
1.3.1 Tujuan umum.....	4
1.3.2 Tujuan khusus.....	4
1.4 Manfaat Penelitian.....	5
1.4.1 Manfaat akademik.....	5
1.4.2 Manfaat praktis.....	5
BAB 2 TINJAUAN KEPUSTAKAAN	
2.1 Karsinoma Urothelial Buli.....	6
2.1.1 Epidemiologi.....	6
2.1.2 Etiologi dan patogenesis.....	7
2.1.3 Gambaran histopatologi.....	9
2.1.3.1 Lesi non invasif.....	11
2.1.3.2 Karsinoma sel urothelial invasif.....	15
2.1.4 Faktor Prognosis.....	16
2.1.4.1 <i>Stage</i> karsinoma urothelial.....	16
2.1.4.2 <i>Grade</i> karsinoma urothelial.....	21
2.1.4.3 Aspek molekular.....	21
2.2 Angiogenesis.....	22
2.2.1 VEGF.....	27
2.2.2 Reseptor VEGF (VEGFR).....	30
2.3 <i>Matrix Methalloproteinase</i> (MMP).....	31
2.3.1 Peranan MMP dalam angiogenesis.....	35
2.3.2 MMP-9.....	36
BAB 3 KERANGKA KONSEPTUAL DAN HIPOTESIS	
3.1 Kerangka Konseptual.....	39
3.2 Hipotesis Penelitian.....	41
BAB 4 METODE PENELITIAN	
4.1 Rancangan Penelitian.....	42
4.2 Populasi dan Sampel Penelitian.....	42

4.2.1 Populasi.....	43
4.2.2 Sampel penelitian.....	43
4.3 Besar Sampel.....	43
4.4 Variabel Penelitian.....	44
4.5 Definisi Operasional.....	44
4.6 Alat dan Bahan Penelitian.....	45
4.6.1 Alat penelitian.....	45
4.6.2 Bahan penelitian.....	46
4.7 Prosedur Penelitian.....	46
4.8 Alur Penelitian.....	47
4.9 Tempat dan Waktu Penelitian.....	47
4.10 Analisis Data.....	48
4.10.1 Analisis deskriptif.....	48
4.10.2 Analisis inferensial.....	48
4.11 Pertimbangan Etik.....	48
4.12 Jadwal Penelitian.....	49
4.13 Lembar Pengumpulan Data.....	49
BAB 5 HASIL PENELITIAN	
5.1 Karakteristik Klinikopatologik Sampel Penelitian.....	50
5.1.1 Distribusi berdasarkan usia.....	50
5.1.2 Distribusi berdasarkan histopatologi.....	51
5.1.3 Distribusi berdasarkan derajat invasi tumor (stadium T)..	52
5.1.4 Distribusi berdasarkan derajat diferensiasi tumor.....	53
5.2 Ekspresi VEGF pada berbagai stadium T karsinoma urothelial buli.....	54
5.3 Ekspresi MMP-9 pada berbagai stadium T karsinoma urothelial buli.....	57
5.4 Korelasi antara ekspresi VEGF dan MMP-9 pada stadium T karsinoma urothelial buli.....	58
BAB 6 PEMBAHASAN	
6.1 Karakteristik Klinikopatologik Sampel Penelitian.....	61
6.2 Ekspresi VEGF pada berbagai stadium T karsinoma urothelial buli.....	64
6.3 Ekspresi MMP-9 pada berbagai stadium T karsinoma urothelial buli.....	68
6.4 Korelasi antara ekspresi VEGF dan MMP-9 pada stadium T karsinoma urothelial buli.....	70
BAB 7 KESIMPULAN DAN SARAN	
7.1 Kesimpulan.....	74
7.2 Saran.....	74
DAFTAR PUSTAKA.....	75
LAMPIRAN.....	83

DAFTAR TABEL

	Halaman
Tabel 2.1 Tumor urothelial berdasarkan WHO	10
Tabel 2.2 Klasifikasi TNM berdasarkan AJCC edisi 8.....	16
Tabel 2.3 Spesifitas substrat dari MMP.....	33
Tabel 4.1 Definisi operasional.....	44
Tabel 4.2 Jadwal penelitian.....	49
Tabel 4.3 Tabel <i>dummy</i> pengumpulan data.....	49
Tabel 5.1 Distribusi kasus berdasarkan jenis histopatologi karsinoma urothelial buli.....	52
Tabel 5.2 Ekspresi VEGF pada stadium T karsinoma urothelial buli.....	54
Tabel 5.3 Ekspresi MMP-9 pada stadium T karsinoma urothelial buli.....	57

DAFTAR GAMBAR

	Halaman
Gambar 2.1 Patogenesis karsinoma urothelial melewati dua jalur berbeda.....	8
Gambar 2.2 Karsinoma urothelial <i>in situ</i>	12
Gambar 2.3 Karsinoma papiler non-invasif.....	13
Gambar 2.4 Penilaian terhadap tumor urothelial papiler non-invasif.....	14
Gambar 2.5 <i>Infiltrating urothelial carcinoma</i>	15
Gambar 2.6 Stadium karsinoma urothelial.....	18
Gambar 2.7 Penilaian stadium T patologik pada karsinoma urothelial.....	20
Gambar 2.8 <i>Angiogenic switch</i>	23
Gambar 2.9 Sinyal HIF-1 α pada kondisi hipoksia.....	25
Gambar 2.10 Fase pembentukan pembuluh darah baru.....	27
Gambar 2.11 Jalur VEGF dan VEGFR.....	32
Gambar 2.12 Struktur domain MMP-9.....	36
Gambar 2.13 Fungsi MMP-9 yang berkaitan dengan pertumbuhan kanker	37
Gambar 3.1 Kerangka konsep penelitian.....	39
Gambar 4.1 Rancangan penelitian.....	42
Gambar 4.2 Alur penelitian.....	47
Gambar 5.1 Distribusi berdasarkan usia.....	51
Gambar 5.2 Distribusi berdasarkan derajat invasi sel tumor (stadium T)	53
Gambar 5.3 Distribusi berdasarkan derajat diferensiasi tumor.....	54
Gambar 5.4 Ekspresi VEGF pada berbagai stadium T karsinoma urotelial buli.....	56
Gambar 5.5 Ekspresi MMP-9 pada berbagai stadium T karsinoma urotelial buli	58

DAFTAR SINGKATAN

AJCC	= <i>American Joint Committee on Cancer</i>
b-FGF	= <i>Basic Fibroblast Growth Factor</i>
bHLH	= <i>Basic Helix-Loop-Helix</i>
DNA	= <i>Deoxyribonucleic Acid</i>
ECM	= <i>Extracellular Matrix</i>
EGF	= <i>Epidermal Growth Factor</i>
EGFR	= <i>Epidermal Growth Factor Receptor</i>
ER	= <i>Estrogen Receptor</i>
ERK	= <i>Extracellular-Signal-Regulated Kinase</i>
FGFR3	= <i>fibroblast growth factor receptor 3</i>
GLOBOCAN	= <i>Global Cancer Observatory</i>
HIF	= <i>Hypoxia-Inducible Factor</i>
HIF-1 α	= <i>Hypoxia-inducible factor 1-alpha</i>
HIF-1 β	= <i>Hypoxia-inducible factor 1-beta</i>
HILPDA	= <i>Hypoxia Inducible Lipid Droplet Associated</i>
LOH	= <i>Lost of Heterozygosity</i>
LSD	= <i>Least Significant Difference</i>
MAPK	= <i>Mitogen activated Protein Kinase</i>
MIBC	= <i>Muscle Invasive Bladder Cancer</i>
MMP	= <i>Matrix Metalloproteinase</i>
NAC	= <i>Neoadjuvant Chemotherapy</i>
NF- κ B	= <i>Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells</i>
NMIBC	= <i>Non Muscle Invasive Bladder Cancer</i>
PDGF	= <i>Platelet-Derived Growth Factor</i>
PDGFR	= <i>Platelet-Derived Growth Factor Receptor</i>
PI3K	= <i>Phosphoinositide 3-kinases</i>
PKC	= <i>Protein kinase C</i>
PLC γ	= <i>Phospholipase C-γ</i>
PIGF	= <i>Placental Growth Factor</i>
PTEN	= <i>Phosphatase and Tensin Homologue</i>
PUNLM	= <i>Papillary Urothelial Neoplasm of Low Malignant Potential</i>
RB	= <i>Retinoblastoma</i>
RhoGDI	= <i>RHO-specific guanine nucleotide dissociation inhibitors</i>
TCGA	= <i>The Cancer Genome Atlas</i>
TGF- β	= <i>Transforming growth factor beta</i>
TIMPs	= <i>Tissue Inhibitors of Metalloproteinases</i>
TIMP-1	= <i>Tissue Inhibitors of Metalloproteinase-1</i>
TNF- α	= <i>Tumor Necrosis Factor alpha</i>
TURBT	= <i>Trans Urethral Resection of Bladder Tumour</i>
VEGF	= <i>Vascular Endothelial Growth Factor</i>
VEGFR	= <i>Vascular Endothelial Growth Factor Receptor</i>
VHL	= <i>Von Hippel-Lindau</i>