

MEKANISME
MOLEKULER TATA LAKSANA
**KANKER
LIDAH**

Siti Rusdiana Puspa Dewi
M. Irsan Saleh
Krisna Murti
Nita Parisa

MEKANISME MOLEKULER TATA LAKSANA KANKER LIDAH

**Siti Rusdiana Puspa Dewi
M. Irsan Saleh
Krisna Murti
Nita Parisa**



PENERBIT KBM INDONESIA

adalah penerbit dengan misi memudahkan proses penerbitan buku-buku penulis di tanah air Indonesia, serta menjadi media *sharing* proses penerbitan buku.

MEKANISME MOLEKULER TATA LAKSANA KANKER LIDAH

Copyright @2025 Siti Rusdiana Puspa Dewi dkk

All right reserved

Penulis

Siti Rusdiana Puspa Dewi

M. Irsan Saleh

Krisna Murti

Nita Parisa

Desain Sampul

Aswan Kreatif

Tata Letak

Husnud Diniyah

Editor

Dr. Muhamad Husein Maruapey, Drs., M.Sc.

Background isi buku di ambil dari <https://www.freepik.com/>

Official

Depok, Sleman-Jogjakarta (Kantor)

Penerbit KBM Indonesia

Anggota IKAPI/No. IKAPI 279/JTI/2021

081357517526 (Tlpn/WA)

Website

<https://penerbitkbm.com>

www.penerbitbukumurah.com

Email

naskah@penerbitkbm.com

Distributor

<https://penerbitkbm.com/toko-buku/>

Youtube

Penerbit KBM Sastrabook

Instagram

@penerbit.kbmindonesia

@penerbitbukujogja

ISBN: 978-634-202-463-8

Cetakan ke-1, Juli 2025

14 x 21 cm, iv + 107 halaman

Isi buku diluar tanggungjawab penerbit
Hak cipta merek KBM Indonesia sudah terdaftar di DJKI-
Kemenkumham dan isi buku dilindungi undang-undang.

Dilarang keras menerjemahkan, memfotokopi, atau
memperbanyak sebagian atau seluruh isi buku ini
tanpa seizin penerbit karena beresiko sengketa hukum

Sanksi Pelanggaran Pasal 113

Undang-Undang No. 28 Tahun 2014 Tentang Hak Cipta

- i. Setiap Orang yang dengan tanpa hak melakukan pelanggaran hak ekonomi sebagaimana dimaksud dalam Pasal 9 ayat (1) huruf i untuk Penggunaan Secara Komersial dipidana dengan pidana penjara paling lama 1 (satu) tahun dan/atau pidana denda paling banyak Rp 100.000.000 (seratus juta rupiah).
- ii. Setiap Orang yang dengan tanpa hak dan/atau tanpa izin Pencipta atau pemegang Hak Cipta melakukan pelanggaran hak ekonomi Pencipta sebagaimana dimaksud dalam Pasal 9 ayat (1) huruf c, huruf d, huruf f, dan/atau huruf h untuk Penggunaan Secara Komersial dipidana dengan pidana penjara paling lama 3 (tiga) tahun dan/atau pidana denda paling banyak Rp 500.000.000,00 (lima ratus juta rupiah).
- iii. Setiap Orang yang dengan tanpa hak dan/atau tanpa izin Pencipta atau pemegang Hak Cipta melakukan pelanggaran hak ekonomi Pencipta sebagaimana dimaksud dalam Pasal 9 ayat (1) huruf a, huruf b, huruf e, dan/atau huruf g untuk Penggunaan Secara Komersial dipidana dengan pidana penjara paling lama 4 (empat) tahun dan/atau pidana denda paling banyak Rp 1.000.000.000,00 (satu miliar rupiah).
- iv. Setiap Orang yang memenuhi unsur sebagaimana dimaksud pada ayat (3) yang dilakukan dalam bentuk pembajakan, dipidana dengan pidana penjara paling lama 10 (sepuluh) tahun dan/atau pidana denda paling banyak Rp 4.000.000.000,00 (empat miliar rupiah).



SURAT PENCATATAN CIPTAAN

Dalam rangka perlindungan ciptaan di bidang ilmu pengetahuan, seni dan sastra berdasarkan Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta, dengan ini menerangkan:

Nomor dan tanggal permohonan

EC002025077376, 27 Juni 2025

Pencipta

Nama : Siti Rusdiana Puspa Dewi, M. Irsan Saleh dkk
Alamat : Jl. Letnan Murod No. 30, Ilir Timur I, Kota Palembang, Sumatera Selatan, 30128
Kewarganegaraan : Indonesia

Pemegang Hak Cipta

Nama : Siti Rusdiana Puspa Dewi, M. Irsan Saleh dkk
Alamat : Jl. Letnan Murod No. 30, Ilir Timur I, Kota Palembang, Sumatera Selatan, 30128
Kewarganegaraan : Indonesia
Jenis Ciptaan : Buku
Judul Ciptaan : MEKANISME MOLEKULER TATA LAKSANA KANKER LIDAH

Tanggal dan tempat diumumkan untuk pertama kali di wilayah Indonesia atau di luar wilayah Indonesia

27 Juni 2025, di Kota Adm. Jakarta Pusat

Jangka waktu perlindungan

Berlaku selama hidup Pencipta dan terus berlangsung selama 70 (tujuh puluh) tahun setelah Pencipta meninggal dunia, terhitung mulai tanggal 1 Januari tahun berikutnya.

Nomor Pencatatan

000917637

adalah benar berdasarkan keterangan yang diberikan oleh Pemohon.

Surat Pencatatan Hak Cipta atau produk Hak terkait ini sesuai dengan Pasal 72 Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta.



a.n. MENTERI HUKUM
DIREKTUR JENDERAL KEKAYAAN INTELEKTUAL
u.p.
Direktur Hak Cipta dan Desain Industri

Agung Damarsasongko, SH, MH.
NIP. 196912261994031001



Disclaimer:

1. Dalam hal pemohon memberikan keterangan tidak sesuai dengan surat pernyataan, Menteri berwenang untuk mencabut surat pencatatan permohonan.
2. Surat Pencatatan ini telah disegel secara elektronik menggunakan segel elektronik yang diterbitkan oleh Balai Besar Sertifikasi Elektronik, Badan Siber dan Sandi Negara.
3. Surat Pencatatan ini dapat dibuktikan keabsahannya dengan memindai kode QR pada dokumen ini dan informasi akan ditampilkan dalam browser.

LAMPIRAN PENCIPTA

No	Nama	Alamat
1	Siti Rusdiana Puspa Dewi	Jl. Letnan Murod No. 30 Ilir Timur I, Kota Palembang
2	M. Irsan Saleh	Jl Sukabangun I Komp. Sarjana Blok B No. 7, Sukajaya Sukarami, Kota Palembang
3	Krisna Murti	Jl. Seruni Komp. Dosen Unsri, Bukit Lama Ilir Barat I, Kota Palembang
4	Nita Parisa	Jl. Darmapala No. 56/57, Bukit Lama Ilir Barat I, Kota Palembang

LAMPIRAN PEMEGANG

No	Nama	Alamat
1	Siti Rusdiana Puspa Dewi	Jl. Letnan Murod No. 30 Ilir Timur I, Kota Palembang
2	M. Irsan Saleh	Jl Sukabangun I Komp. Sarjana Blok B No. 7, Sukajaya Sukarami, Kota Palembang
3	Krisna Murti	Jl. Seruni Komp. Dosen Unsri, Bukit Lama Ilir Barat I, Kota Palembang
4	Nita Parisa	Jl. Darmapala No. 56/57, Bukit Lama Ilir Barat I, Kota Palembang



KATA PENGANTAR

Assalamualaikum Warahmatullahi Wabarakatuh.

Segala puji dan syukur atas kehadiran Allah SWT karena atas karunia, rahmat, taufik, dan hidayah-Nya sehingga monograf ini dapat diselesaikan dengan baik. Monograf ini dibuat untuk memberikan informasi mengenai mekanisme molekular dalam tata laksana kanker pada lidah. Kanker pada lidah merupakan suatu jenis kanker yang menjadi penyebab kematian yang tinggi dari semua kanker rongga mulut.

Monograf ini disusun untuk membantu menambah referensi mengenai mekanisme molekular dari kanker lidah beserta tata laksananya. Monograf ini juga dapat digunakan oleh seluruh segmen masyarakat sehingga dapat memberikan kontribusi positif dalam proses pembelajaran.

Monograf ini membahas mengenai kanker lidah, sejarah kanker lidah, mekanisme molekular target terapi kanker lidah yang dapat. Monograf ini juga berisi mengenai penjelasan terkait mengenai terapi anti kanker yang dapat berpotensi untuk dapat dikembangkan di masa depan.

Penulis menyadari bahwa dalam penyusunan monograf ini masih terdapat banyak kekurangan. Oleh

karena itu penulis berkenan dalam menerima segala kritik, saran, dan masukan secara terbuka dan bersifat membangun.

Besar harapan penulis bahwa monograf ini dapat memberikan manfaat bagi banyak orang.

Palembang, Mei 2025

Penulis

DAFTAR ISI

KATA PENGANTAR	i
DAFTAR ISI	iii
BAB 1 KANKER LIDAH	1
1.1 Latar Belakang	1
1.2 Tahapan Perkembangan Kanker Lidah.....	6
1.3 Jenis-Jenis Kanker Lidah	9
1.3.1 Karsinoma Sel Skuamosa Subtipe Konvensional	9
1.3.2 Karsinoma Sel Skuamosa Subtipe Basaloid.....	10
1.3.3 Karsinoma Sel Skuamosa Subtipe Sel Spindel.....	10
1.3.4 Karsinoma Sel Skuamosa Subtipe Adenoskuamosa.....	12
1.3.5 Karsinoma Sel Skuamosa Subtipe Kunikulatum.....	12
1.3.6 Karsinoma Sel Skuamosa Subtipe Verukosa.....	13
1.3.7 Karsinoma Sel Skuamosa Subtipe Limfoepitelial.....	14
1.3.8 Karsinoma Sel Skuamosa Subtipe Akantolitik.....	15
BAB 2 SEJARAH	17

BAB 3 TATA LAKSANA KANKER LIDAH.....	25
3.1 Tatalaksana Kanker Lidah.....	25
3.1.1 Pembedahan.....	26
3.1.2 Terapi Radiasi.....	27
3.1.3 Kemoterapi.....	28
3.1.4 Immunoterapi.....	31
3.1.5 Obat-Obatan Alternatif.....	34
3.2 Mekanisme Molekular Target Terapi.....	38
3.2.1 Apoptosis.....	38
3.2.2 Inhibisi Siklus Sel	43
3.2.3 Anti Proliferasi	44
3.2.4 Penghambatan Angiogenesis dan Limfangiogenesis.....	46
3.2.5 Anti Metastasis.....	48
3.3 Pengobatan Modern Kanker Lidah	51
3.3.1 Protein Sebagai Target Terapi Kanker	62
3.3.1.1 <i>Vascular Endothelial Growth Factor</i> <i>Receptor</i> (VEGFR).....	62
3.3.1.2 <i>Epidermal Growth Factor Receptor</i> (EGFR).....	65
3.3.1.3 Fas Reseptor	69
3.3.1.4 BCl-2	74
3.3.2 <i>Docking</i> Molekuler.....	74
3.4 Efek Samping Tata Laksana Terapi Kanker Lidah.....	83
BAB 4 SIMPULAN.....	87
DAFTAR PUSTAKA.....	89

DAFTAR PUSTAKA

- Aamir R, Rauf F, Iqbal F, Yousuf S, Rehman A, Sheikh AK, Muhammad S. Immunohistochemical expression of epidermal growth factor receptor (EGFR) in oral squamous cell carcinoma and oral potentially malignant disorders. *Appl Immunohistochem Mol Morphol*. 2024 Mar 1;32(3):157-162. doi: 10.1097/PAI.0000000000001185.
- Abergel R, Aris J, Bolch WE, Dewji SA, Golden A, Hooper DA, Margot D, Menker CG, Paunesku T, Schaue D, Woloschak GE. The enduring legacy of Marie Curie: impacts of radium in 21st century radiological and medical sciences. *Int J Radiat Biol*. 2022;98(3):267-275. doi: 10.1080/09553002.2022.2027542. Epub 2022 Feb 2. PMID: 35030065; PMCID: PMC9723808.
- Abourehab MAS, Alqahtani AM, Youssif BGM, Gouda AM. *Globally approved egfr inhibitors: insights into their syntheses, target kinases, biological activities, receptor interactions, and metabolism*. *Molecules*. 2021 Nov 4;26(21):6677. doi: 10.3390/molecules26216677.
- Agrawal AG, Hande AH, Bansod A, Goenka Y, Panchabhai A. Role of Epidermal Growth Factor (EGFR) in Oral Cancer. *J. Pharm. Res. Int.* [Internet]. 2021 Dec. 28 [cited 2024 Dec. 21];33(61B):78-84. Available from:

<https://journaljpri.com/index.php/JPRI/article/view/5397>

- Agu PC, Afiukwa CA, Orji OU, Ezech EM, Ofoke IH, Ogbu CO, Ugwuja EI, Aja PM. Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. *Sci Rep.* 2023 Aug 17;13(1):13398. doi: 10.1038/s41598-023-40160-2.
- Altun İ, Sonkaya A. The Most Common Side Effects Experienced by Patients Were Receiving First Cycle of Chemotherapy. *Iran J Public Health.* 2018 Aug;47(8):1218-1219. PMID: 30186799; PMCID: PMC6123577.
- Altun İ, Sonkaya A. The Most Common Side Effects Experienced by Patients Were Receiving First Cycle of Chemotherapy. *Iran J Public Health.* 2018 Aug;47(8):1218-1219. PMID: 30186799; PMCID: PMC6123577.
- Avdeef A, Kansy M. "flexible-acceptor" general solubility equation for beyond rule of 5 drugs. *Mol Pharm.* 2020 Oct 5;17(10):3930-3940. doi: 10.1021/acs.molpharmaceut.0c00689.
- Benjamin O, Goyal A, Lappin SL. *Disease-Modifying Antirheumatic Drugs (DMARD)* [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK507863/>
- Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024 ; 74(3): 229-63. doi: 10.3322/caac.21834.

- Burus T, Damgacioglu H, Huang B, Christian WJ, Hull PC, Ellis AR, Arnold SM, Deshmukh AA, Kuhs KAL. Recent and projected trends in oral tongue cancer in the united states: a demographic shift in case burden as early onset increases among females subsides. *Res Sq* 2023; 3; 3359293. doi: 10.21203/rs.3.rs-3359293/v1.
- Carpenter LC, Pérez-Verdugo F, Banerjee S. *Mechanical control of cell proliferation patterns in growing tissues*. bioRxiv [Preprint]. 2023 Jul 27:2023.07.25.550581. doi: 10.1101/2023.07.25.550581.
- Chaudhry GE, Akim AM, Sung YY, Muhammad TST. Cancer and Apoptosis. *Methods Mol Biol*. 2022;2543:191-210. doi: 10.1007/978-1-0716-2553-8_16.
- Chung S, Yi Y, Ullah I, Chung K, Park S, Lim J, Kim C, Pyun SH, Kim M, Kim D. Systemic treatment with Fas-blocking peptide attenuates apoptosis in brain ischemia. *Int. J. Mol. Sci*. 2024;25:661. <https://doi.org/10.3390/ijms25010661>
- Cívico-Ortega JL, González-Ruiz I, Ramos-García P, Cruz-Granados D, Samayoa-Descamps V, González-Moles MÁ. Prognostic and Clinicopathological Significance of Epidermal Growth Factor Receptor (EGFR) Expression in Oral Squamous Cell Carcinoma: Systematic Review and Meta-Analysis. *International Journal of Molecular Sciences*. 2023; 24(15):11888. <https://doi.org/10.3390/ijms241511888>
- Clifton LA, Wacklin-Knecht HP, Ådén J, Mushtaq AU, Sparrman T, Gröbner G. Creation of distinctive Bax-lipid complexes at mitochondrial membrane surfaces drives pore formation to initiate apoptosis. *Sci Adv*.

- 2023 Jun 2;9(22):eadg7940. doi: 10.1126/sciadv.adg7940.
- Colditz GA, Bohlke K, Berkey CS. Breast cancer risk accumulation starts early: prevention must also. *Breast Cancer Res Treat.* 2014 Jun;145(3):567-79. doi: 10.1007/s10549-014-2993-8. Epub 2014 May 13. PMID: 24820413; PMCID: PMC4079839.
- Consonni F, Gambineri E, Favre C. ALPS, FAS, and beyond: from inborn errors of immunity to acquired immunodeficiencies. *Ann Hematol.* 2022 Mar;101(3):469-484. doi: 10.1007/s00277-022-04761-7.
- Dauids MS. Targeting BCL-2 in B-cell lymphomas. *Blood.* 2017 Aug 31;130(9):1081-1088. doi: 10.1182/blood-2017-04-737338.
- Dewi SRP, Marlamsya DO, Bikarindrasari R. Efek antikaries ekstrak gambir pada tikus jantan galur wistar. *Maj Kedokt Gigi Indones.* 2017;3(2):83.
- Dobosz P, Dzieciatkowski T. The Intriguing History of Cancer Immunotherapy. *Front. Immunol.* 2019;10:2965
- Elmore S. Apoptosis: a review of programmed cell death. *Toxicol Pathol.* 2007 Jun;35(4):495-516. doi: 10.1080/01926230701320337.
- Fares J, Fares MY, Khachfe HH. Molecular principles of metastasis: a hallmark of cancer revisited. *Sig Transduct Target Ther.* 2020;5:28. <https://doi.org/10.1038/s41392-020-0134-x>
- Gandalovičová A, Rosel D, Fernandes M, Veselý P, Heneberg P, Čermák V, Petruželka L, Kumar S, Sanz-Moreno V, Brábek J. Migrastatics-Anti-metastatic and Anti-invasion Drugs: Promises and Challenges.

- Trends Cancer*. 2017 Jun;3(6):391-406. doi: 10.1016/j.trecan.2017.04.008. PMID: 28670628; PMCID: PMC5482322.
- Gianfaldoni S, Gianfaldoni R, Wollina U, Lotti J, Tchernev G, Lotti T. An Overview on Radiotherapy: From Its History to Its Current Applications in Dermatology. *Open Access Maced J Med Sci*. 2017 Jul 18;5(4):521-525. doi: 10.3889/oamjms.2017.122. PMID: 28785349; PMCID: PMC5535674.
- Gonzalez M, March AR. *Tongue Cancer*. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK562324/>
- Hans S, Baudouin R, Circiu MP, Couineau F, Lisan Q, Crevier-Buchman L, Lechien JR. Open Partial Laryngectomies: History of Laryngeal Cancer Surgery. *J Clin Med*. 2022 Sep 12;11(18):5352. doi: 10.3390/jcm11185352. PMID: 36142999; PMCID: PMC9501694.
- Hidayat R, Hayati L. Regulation of Cell Cycle. *Biomedical Journal of Indonesia* 2020; 6(3):84-90
- Huang L, Zhang C. Microscale thermophoresis (MST) to detect the interaction between purified protein and small molecule. *Methods Mol Biol*. 2021;2213:187-193. doi: 10.1007/978-1-0716-0954-5_17.
- Hussain S, Alhadidi QM. Polyphenols as Tyrosine Kinase Inhibitors for the Treatment of Metastatic Cancers: Current and Future Perspective. *Indonesian Journal of Pharmacy*, 2022;33(3):366-380. <https://doi.org/10.22146/ijp.3844>
- Hussain S, Alhadidi QM. Polyphenols as Tyrosine Kinase Inhibitors for the Treatment of Metastatic Cancers:

- Current and Future Perspective. *Indonesian Journal of Pharmacy* 2002;33(3):366-380.
<https://doi.org/10.22146/ijp.3844>
- Hussar P. *Pengatur apoptosis Bcl-2 dan Caspase-3*. Ensiklopedia 2022; 2: 1624-36.
<https://doi.org/10.3390/encyclopedia2040111>
- Imbesi Bellantoni M, Picciolo G, Pirrotta I, Irrera N, Vaccaro M, Vaccaro F, Squadrito F, Pallio G. Oral cavity squamous cell carcinoma: an update of the pharmacological treatment. *biomedicines*. 2023 Apr 7;11(4):1112. doi: 10.3390/biomedicines11041112.
- Inchingolo F, Santacroce L, Ballini A, Topi S, Dipalma G, Haxhirexha K, Bottalico L, Charitos IA. Oral Cancer: A Historical Review. *Int J Environ Res Public Health*. 2020 May 2;17(9):3168. doi: 10.3390/ijerph17093168. PMID: 32370133; PMCID: PMC7246763.
- Ion Ciucă Mărășescu FI, Marasescu PC, Matei M, Florescu AM, Margaritescu C, Petrescu SMS, Dumitrescu CI. Epidemiological and histopathological aspects of tongue squamous cell carcinomas-retrospective study. *Curr Health Sci J*. 2018 Jul-Sep;44(3):211-224. doi: 10.12865/CHSJ.44.03.03.
- Ion Ciucă Mărășescu FI, Marasescu PC, Matei M, Florescu AM, Margaritescu C, Petrescu SMS, Dumitrescu CI. Epidemiological and histopathological aspects of tongue squamous cell carcinomas-retrospective study. *Curr Health Sci J*. 2018 Jul-Sep;44(3):211-224. doi: 10.12865/CHSJ.44.03.03.
- Irani S. New Insights into Oral Cancer-Risk Factors and Prevention: A Review of Literature. *Int J Prev Med*.

- 2020 Dec 30;11:202. doi: 10.4103/ijpvm.IJPVM_403_18.
- Ivanova L, Karelson M. The impact of software used and the type of target protein on molecular docking accuracy. *Molecules*. 2022 Dec 18;27(24):9041. doi: 10.3390/molecules27249041.
- Iyengar SM, Barnsley KK, Xu R, Prystupa A, Ondrechen MJ. Electrostatic fingerprints of catalytically active amino acids in enzymes. *Protein Sci*. 2022 May;31(5):e4291. doi: 10.1002/pro.4291.
- Jan R, Chaudhry GE. Understanding Apoptosis and Apoptotic Pathways Targeted Cancer Therapeutics. *Adv Pharm Bull*. 2019 Jun;9(2):205-218. doi: 10.15171/apb.2019.024. Epub 2019 Jun 1. PMID: 31380246; PMCID: PMC6664112.
- Jhunjhunwala S, Hammer C, Delamarre L. Antigen presentation in cancer: insights into tumour immunogenicity and immune evasion. *Nat Rev Cancer* 2021;21:298–312. <https://doi.org/10.1038/s41568-021-00339-z>
- Jones D. Parallels of Resistance between Angiogenesis and Lymphangiogenesis Inhibition in Cancer Therapy. *Cells*. 2020 Mar 20;9(3):762. doi: 10.3390/cells9030762. PMID: 32244922; PMCID: PMC7140636.
- Kanter GP, Ozluk P, Chi W. Cancer Treatment Before and After Physician-Pharmacy Integration. *JAMA Netw Open*. 2024;7(5):e2412998. doi:10.1001/jamanetworkopen.2024.12998
- Karami TK, Hailu S, Feng S, Graham R, Gukasyan HJ. Eyes on Lipinski's Rule of Five: A new "rule of thumb" for physicochemical design space of ophthalmic drugs. *J*

- Ocul Pharmacol Ther.* 2022 Jan-Feb;38(1):43-55. doi: 10.1089/jop.2021.0069.
- Katta B, Vijayakumar C, Dutta S, Dubashi B, Nelamangala Ramakrishnaiah VP. The Incidence and Severity of Patient-Reported Side Effects of Chemotherapy in Routine Clinical Care: A Prospective Observational Study. *Cureus.* 2023 Apr 29;15(4):e38301. doi: 10.7759/cureus.38301. PMID: 37261144; PMCID: PMC10226821.
- Khalid N, Azimpouran M. *Necrosis*. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
- Kim MG, Choi YS, Youn SM, Ko JH, Oh HJ, Lee JH, Park JY, Choi SW. Treatment outcomes and prognostic factors in oral tongue cancer: a 20-year retrospective study at the National Cancer Center, South Korea. *J Korean Assoc Oral Maxillofac Surg.* 2022 ;48(4):192-200. doi: 10.5125/jkaoms.2022.48.4.192.
- Korablev AV, Sesorova IS, Sesorov VV, Vavilov PS, Mironov A, Zaitseva AV, Bedyayev EV, Mironov AA. New Interpretations for Sprouting, Intussusception, Ansiform, and Coalescent Types of Angiogenesis. *International Journal of Molecular Sciences.* 2024; 25(16):8575.
<https://doi.org/10.3390/ijms25168575>
- Kumar M, Nanavati R Modi TG, Dobariya C. Oral cancer: etiology and risk factors. *Journal of Cancer Research and Therapeutics* 2016; 12(2): 458-63 DOI: 10.4103/0973-1482.186696
- Kumar SS, McGarry RC. Management of local recurrences and regional failure in early stage non-small cell lung cancer after stereotactic body radiation therapy.

Translational Lung Cancer Research, 2019; 8(2):254-277

- Kuznetsova AA, Fedorova OS, Kuznetsov NA. Structural and Molecular Kinetic Features of Activities of DNA Polymerases. *Int J Mol Sci*. 2022 Jun 7;23(12):6373. doi: 10.3390/ijms23126373. PMID: 35742812; PMCID: PMC9224347.
- Kuznetsova AA, Fedorova OS, Kuznetsov NA. Structural and Molecular Kinetic Features of Activities of DNA Polymerases. *Int J Mol Sci*. 2022 Jun 7;23(12):6373. doi: 10.3390/ijms23126373. PMID: 35742812; PMCID: PMC9224347.
- Kyriazi D, Voth L, Bader A, Ewert W, Gerlach J, Elfrink K, Franz P, Tsap MI, Schirmer B, Damiano-Guercio J, Hartmann FK, Plenge M, Salari A, Schöttelndreier D, Strienke K, Bresch N, Salinas C, Gutzeit HO, Schaumann N, Hussein K, Bähre H, Brüschi I, Claus P, Neumann D, Taft MH, Shcherbata HR, Ngezahayo A, Bähler M, Amiri M, Knölker HJ, Preller M, Tsiavalariis G. An allosteric inhibitor of RhoGAP class-IX myosins suppresses the metastatic features of cancer cells. *Nat Commun*. 2024 Nov 16;15(1):9947. doi: 10.1038/s41467-024-54181-6. PMID: 39550360; PMCID: PMC11569205.
- Landau MB, Abdelmaksoud A, Hussein MH, Jishu JA, Fawzy MS, Toraih EA, Kandil E. Reviving ancient therapeutics in modern medicine: an immunological and biological narrative review of wet cupping in the management of Hashimoto's thyroiditis. *Gland Surgery*. 2024;13(7)
- Lemaire J, Larrue R, Perrais M, Cauffiez C, Pottier N. Aspects fondamentaux du développement tumoral

- [Fundamental aspects of oncogenesis]. *Bull Cancer*. 2020 Nov;107(11):1148-1160. French. doi: 10.1016/j.bulcan.2020.08.004. Epub 2020 Oct 7. PMID: 33039132.
- Li LJ, Chang PM, Li CH, Chang YC, Lai TC, Su CY, Chen CL, Chang WM, Hsiao M, Feng SW. FAS receptor regulates NOTCH activity through ERK-JAG1 axis activation and controls oral cancer stemness ability and pulmonary metastasis. *Cell Death Discov*. 2022 Mar 5;8(1):101. doi: 10.1038/s41420-022-00899-5.
- Lipinski CA, Reaume AG. Phenotypic screening of low molecular weight compounds is rich ground for repurposed, on-target drugs. *Front Pharmacol*. 2022 Aug 8;13:917968. doi: 10.3389/fphar.2022.917968.
- Liu JC, Sopka DS, Mehra R, Lango MN, Fundakowski C, Ridge JA, Galloway TJ. Early oral tongue cancer initially managed with surgery alone: Treatment of recurrence. *World J Otorhinolaryngol Head Neck Surg*. 2016 May 5;2(4):193-197. doi: 10.1016/j.wjorl.2016.03.001. PMID: 29204565; PMCID: PMC5698535.
- Liu ZL, Chen HH, Zheng LL, Sun LP, Shi L. Angiogenic signaling pathways and anti-angiogenic therapy for cancer. *Signal Transduct Target Ther*. 2023 May 11;8(1):198. doi: 10.1038/s41392-023-01460-1. PMID: 37169756; PMCID: PMC10175505.
- Malmir N, Fard NA, Mgwatyu Y, Mekuto L. *Cyanide hydratase* modification using computational design and docking analysis for improved binding affinity in cyanide detoxification. *Molecules*. 2021 Mar 23;26(6):1799. doi: 10.3390/molecules26061799.

- Mastuo T, Miyata Y, Yuno T, Mukae Y, Otsubo A, Mitsunari K, Ohba K, Sakai H. Molecular Mechanisms of the Anti-Cancer Effects of Isothiocyanates from Cruciferous Vegetables in Bladder Cancer. *Molecules*. 2020 Jan 29;25(3):575. doi: 10.3390/molecules25030575. PMID: 32013065; PMCID: PMC7037050.
- Matsuo K, Akiba J, Kusukawa J, Yano H. Squamous cell carcinoma of the tongue: subtypes and morphological features affecting prognosis. *Am J Physiology-Cell Phy*. 2022;323(6):1611-1623
- McAleer S. A history of cancer and its treatment: Presidential Address to the Ulster Medical Society. 7th October 2021. *Ulster Med J*. 2022 Sep;91(3):124-129. Epub 2022 Dec 5. PMID: 36474852; PMCID: PMC9720583.
- Migueláñez-Medrán BC, Pozo-Kreilinger JJ, Cebrián-Carretero JL, Martínez-García MA, López-Sánchez AF. Oral squamous cell carcinoma of tongue: Histological risk assessment. A pilot study. *Med Oral Patol Oral Cir Bucal*. 2019 Sep 1;24(5):e603-e609. doi: 10.4317/medoral.23011.
- Modi SJ, Kulkarni VM. Vascular Endothelial Growth Factor Receptor (VEGFR-2)/KDR Inhibitors: Medicinal Chemistry Perspective. *Medicine in Drug Discovery* 2019;2(2): 1-12. <https://doi.org/10.1016/j.medidd.2019.100009>.
- Mohan SP, Bhaskaran MK, George AL, Thirutheri A, Somasundaran M, Pavithran A. Immunotherapy in Oral Cancer. *J Pharm Bioallied Sci*. 2019 May;11(Suppl 2):S107-S111. doi:

10.4103/JPBS.JPBS_31_19. PMID: 31198321; PMCID: PMC6555318.

Mohan SP, Bhaskaran MK, George AL, Thirutheri A, Somasundaran M, Pavithran A. Immunotherapy in Oral Cancer. *J Pharm Bioallied Sci.* 2019 May;11(Suppl 2):S107-S111. doi: 10.4103/JPBS.JPBS_31_19. PMID: 31198321; PMCID: PMC6555318.

Nasser H, St John MA. The promise of immunotherapy in the treatment of young adults with oral tongue cancer. *Laryngoscope Investig Otolaryngol.* 2020 Feb 21;5(2):235-242. doi: 10.1002/lio2.366. PMID: 32337355; PMCID: PMC7178456.

Nasser H, St John MA. The promise of immunotherapy in the treatment of young adults with oral tongue cancer. *Laryngoscope Investig Otolaryngol.* 2020 Feb 21;5(2):235-242. doi: 10.1002/lio2.366. PMID: 32337355; PMCID: PMC7178456.

Nazhvani AD, Sarafranz N, Askari F, Heidari F, Razmkhah M. Anti-cancer effects of traditional medicinal herbs on oral squamous cell carcinoma. *Asian Pac J Cancer Prev.* 2020 Feb 1;21(2):479-484. doi: 10.31557/APJCP.2020.21.2.479.

Ni B, Wang H, Khalaf HKS, Blay V, Houston DR. AutoDock-SS: AutoDock for Multiconformational Ligand-Based Virtual Screening. *J Chem Inf Model.* 2024 May 13;64(9):3779-3789. doi: 10.1021/acs.jcim.4c00136.

Nova R, Hoemardani ASD, Louisa M. Potential of herbal medicine in cancer therapy. *The Indonesia Journal of Cancer Control* 2021;1(1): 44-50.

Paladini A, Barrientos Penaloza J, Plancarte Sanchez R, Ergönenç T, Varrassi G. Bridging Old and New in Pain

- Medicine: An Historical Review. *Cureus*. 2023 Aug 17;15(8):e43639. doi: 10.7759/cureus.43639. PMID: 37719480; PMCID: PMC10504912.
- Park YM, Lim JY, Koh YW, Kim SH, Choi EC. Long-term outcomes of early stage oral tongue cancer: Main cause of treatment failure and second primary malignancy. *Laryngoscope Investig Otolaryngol*. 2022;7(6):1830-1836. doi: 10.1002/lio2.943.
- Park YM, Lim JY, Koh YW, Kim SH, Choi EC. Long-term outcomes of early stage oral tongue cancer: Main cause of treatment failure and second primary malignancy. *Laryngoscope Investig Otolaryngol*. 2022;7(6):1830-1836. doi: 10.1002/lio2.943.
- Permatasanti A, Hidayat W. Potential of Indonesian Herbal as an Anti-Cancer Therapy: A Systemic Review of in vitro Studies. *Cancer Manag Res*. 2023 Aug 17;15:837-850. doi: 10.2147/CMAR.S414457.
- Pfeffer CM, Singh ATK. Apoptosis: A target for anticancer therapy. *Int J Mol Sci*. 2018 Feb 2;19(2):448. doi: 10.3390/ijms19020448
- Pinzi L, Rastelli G. Molecular Docking: Shifting Paradigms in Drug Discovery. *International Journal of Molecular Sciences*. 2019; 20(18):4331. <https://doi.org/10.3390/ijms20184331>.
- Prior IA, Lewis PD, Mattos C. A comprehensive survey of Ras mutations in cancer. *Cancer Res*. 2012 May 15;72(10):2457-67. doi: 10.1158/0008-5472.CAN-11-2612. PMID: 22589270; PMCID: PMC3354961.
- Raval K, Ganatra T. Basics, types and applications of molecular docking: A review. *IP International Journal of Comprehensive and Advanced Pharmacology* 2022;7(1):12-16.

- Ren Y, Zhang Y, Liu J, Liu P, Yang J, Guo D, Tang A, Tao J. Matrix hardness regulates the cancer cell malignant progression through cytoskeletal network. *Biochemical and Biophysical Research Communications*. 2021; 542: 95-101.
- Rosen RD, Sapra A. *TNM Classification*. [Updated 2023 Feb 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK553187/>
- Roskoski R Jr. Rule of five violations among the FDA-approved small molecule protein kinase inhibitors. *Pharmacol Res*. 2023 May;191:106774. doi: 10.1016/j.phrs.2023.106774.
- Routh ED, Beckabir W, Vensko SP, Serody JS, Vincent BG. Evaluation of tumor antigen-specific antibody responses in patients with metastatic triple negative breast cancer treated with cyclophosphamide and pembrolizumab. *Journal for ImmunoTherapy of Cancer* 2023;11:e005848. doi: 10.1136/jitc-2022-005848
- Sakr Y, Hamdy O, Eldeghedi M, Abdelaziz R, El Moctar EMS, Alharazin M, Awny S. *Shifting epidemiology trends in tongue cancer: a retrospective cohort study*. *Cancers* 2023; 15: 5680. <https://doi.org/10.3390/cancers15235680>
- Sankaranarayanan R, Ramadas K, Amarasinghe H. Oral Cancer: Prevention, Early Detection, and Treatment. In: Gelband H, Jha P, Sankaranarayanan R, et al., editors. *Cancer: Disease Control Priorities, Third Edition* (Volume 3). Washington (DC): The International Bank for Reconstruction and

- Development / The World Bank; 2015 Nov 1. Chapter 5.
- Shah AA, Kamal MA, Akhtar S. Tumor Angiogenesis and VEGFR-2: Mechanism, pathways and current biological therapeutic interventions. *Curr Drug Metab.* 2021;22(1):50-59. doi: 10.2174/1389200221666201019143252.
- Shah M, Mortazavi A, Folefac E, Wang P, Collier KA, Meng L, Slavens K, Hinkley M, Monk III P, Bond DA. Decade of insights: Bleomycin-induced pneumonitis and use of G-CSF in chemotherapy-treated germ cell testicular tumors and Hodgkin lymphoma—Real-world outcomes from an academic cancer center.. *J Clin Onco* 2024;42:e17013-e17013(2024).
- Simanshu DK, Nissley DV, McCormick F. RAS Proteins and Their Regulators in Human Disease. *Cell.* 2017 Jun 29;170(1):17-33. doi: 10.1016/j.cell.2017.06.009. PMID: 28666118; PMCID: PMC5555610.
- Singh D, Attri BK, Gill RK, Bariwal J. Review on EGFR Inhibitors: Critical Updates. *Mini Rev Med Chem.* 2016;16(14):1134-66. doi: 10.2174/1389557516666160321114917.
- Singh RK, Kumar S, Prasad DN, Bhardwaj TR. Therapeutic journey of nitrogen mustard as alkylating anticancer agents: Historic to future perspectives. *Eur J Med Chem.* 2018 May 10;151:401-433. doi: 10.1016/j.ejmech.2018.04.001. Epub 2018 Apr 3. PMID: 29649739.
- Soliman TN, Keifenheim D, Parker PJ, Clarke DJ. Cell cycle responses to Topoisomerase II inhibition: Molecular mechanisms and clinical implications. *J Cell Biol.* 2023 Dec 4;222(12):e202209125. doi:

- 10.1083/jcb.202209125. Epub 2023 Nov 13. PMID: 37955972; PMCID: PMC10641588.
- Stachowski TR, Fischer M. Large-Scale ligand perturbations of the protein conformational landscape reveal state-specific interaction hotspots. *J Med Chem*. 2022 Oct 27;65(20):13692-13704. doi: 10.1021/acs.jmedchem.2c00708.
- Stewart BW. Mechanisms of carcinogenesis: from initiation and promotion to the hallmarks. In: Baan RA, Stewart BW, Straif K, editors. *Tumour Site Concordance and Mechanisms of Carcinogenesis. Lyon (FR): International Agency for Research on Cancer; 2019. (IARC Scientific Publications, No. 165.) Chapter 11. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK570326/>*
- Sui B, Wang R, Chen C, Kou X, Wu D, Fu Y, Lei F, Wang Y, Liu Y, Chen X, Xu H, Liu Y, Kang J, Liu H, Kwok RTK, Tang BZ, Yan H, Wang M, Xiang L, Yan X, Zhang X, Ma L, Shi S, Jin Y. *Apoptotic vesicular metabolism contributes to organelle assembly and safeguards liver homeostasis and regeneration. Gastroenterology*. 2024 Jul;167(2):343-356. doi: 10.1053/j.gastro.2024.02.001.
- Sultana J, Bashar A, Molla MR. New Management Strategies of Oral Tongue Cancer in Bangladesh. *J Maxillofac Oral Surg*. 2014 Dec;13(4):394-400. doi: 10.1007/s12663-013-0566-8. Epub 2013 Aug 30. PMID: 26225002; PMCID: PMC4518807.
- Szwabowski GL, Griffing M, Mugabe EJ, O'Malley D, Baker LN, Baker DL, Parrill AL. G protein-coupled receptor-ligand pose and functional class prediction. *Int J Mol*

- Sci.* 2024 Jun 22;25(13):6876. doi: 10.3390/ijms25136876.
- Talukdar S, Emdad L, Das SK, Fisher PB. EGFR: An essential receptor tyrosine kinase-regulator of cancer stem cells. *Adv Cancer Res.* 2020;147:161-188. doi: 10.1016/bs.acr.2020.04.003.
- Tan YS, Chakrabarti M, Stein RM, Prentis LE, Rizzo RC, Kurtzman T, Fischer M, Balias TE. Development of receptor desolvation scoring and covalent sampling in dock 6: methods evaluated on a RAS test set. *J Chem Inf Model.* 2025 Jan 27;65(2):722-748. doi: 10.1021/acs.jcim.4c01623.
- Tonnus W, Meyer C, Paliege A, Belavgeni A, von Mässenhausen A, Bornstein SR, Hugo C, Becker JU, Linkermann A. *The pathological features of regulated necrosis.* 2019; 247(5):697-707
- Torres PHM, Sodero ACR, Jofily P, Silva-Jr FP. Key Topics in molecular docking for drug design. *Int J Mol Sci.* 2019 Sep 15;20(18):4574. doi: 10.3390/ijms20184574.
- Uba AI. Computer-Aided Design of VEGFR-2 Inhibitors as Anticancer Agents: A Review. *J Mol Recognit.* 2025 Jan;38(1):e3104. doi: 10.1002/jmr.3104.
- Vasques AC Sr, Cavaco P, Duarte T, Duarte Branco V, Miranda Baleiras M, Pinto M, Ferreira F, Falcão MF, Dias Domingues T, Martins A. The Use of Herbal Medicines Among Cancer Patients. *Cureus.* 2024 Feb 2;16(2):e53455. doi: 10.7759/cureus.53455.
- Wang, H., Guo, M., Wei, H. et al. Targeting p53 pathways: mechanisms, structures and advances in therapy. *Sig Transduct Target Ther* 8, 92 (2023). <https://doi.org/10.1038/s41392-023-01347>

- Watson J, Ninh MK, Ashford S, Cornett EM, Kaye AD, Urits I, Viswanath O. Anesthesia Medications and Interaction with Chemotherapeutic Agents. *Oncol Ther*. 2021 Jun;9(1):121-138. doi: 10.1007/s40487-021-00149-1. Epub 2021 Apr 16. PMID: 33861416; PMCID: PMC8140172.
- Watson J, Ninh MK, Ashford S, Cornett EM, Kaye AD, Urits I, Viswanath O. Anesthesia Medications and Interaction with Chemotherapeutic Agents. *Oncol Ther*. 2021 Jun;9(1):121-138. doi: 10.1007/s40487-021-00149-1. Epub 2021 Apr 16. PMID: 33861416; PMCID: PMC8140172.
- Westaby D, Jimenez-Vacas JM, Padilha A, Varkaris A, Balk SP, de Bono JS, Sharp A. Targeting the Intrinsic Apoptosis Pathway: A Window of Opportunity for Prostate Cancer. *Cancers* 2022; 14; 51. <https://doi.org/10.3390/cancers14010051>
- Williams AB, Schumacher B. p53 in the DNA-Damage-Repair Process. *Cold Spring Harb Perspect Med*. 2016 May 2;6(5):a026070. doi: 10.1101/cshperspect.a026070. PMID: 27048304; PMCID: PMC4852800.
- Yanumula A, Cusick JK. Biochemistry, *Extrinsic Pathway of Apoptosis*. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK560811/>
- Zhang Y, Li S, Meng K, Sun S. Machine learning for sequence and structure-based protein-ligand interaction prediction. *J Chem Inf Model*. 2024 Mar 11;64(5):1456-1472. doi: 10.1021/acs.jcim.3c01841. Epub 2024 Feb 22. Erratum in: *J Chem Inf Model*.

2024 Oct 14;64(19):7826. doi:
10.1021/acs.jcim.4c01662.

Zheng S, Xu S, Wang G, Tang Q, Jiang X, Li Z, Xu Y, Wang R, Lin F. Proposed hydrogen-bonding index of donor or acceptor reflecting its intrinsic contribution to hydrogen-bonding strength. *J Chem Inf Model*. 2017 Jul 24;57(7):1535-1547. doi:
10.1021/acs.jcim.7b00022.