

7. References

1. Gray's anatomy: The anatomical basis of clinical practice 41st edition.
2. Medzhitov R. Origin and physiological roles of inflammation. *Nature*. **2008**, 454, 428–435.
3. Anderson D.; Novak P.; Keith J.; Elliott M.; Saunders WB.; Philidelphia Co. *Dorland's Illustrated Medical Dictionary*. **2004**, 13 (3), 326.
4. Carroll MC. A protective role for innate immunity in autoimmune disease. *Clinical Immunology*. **2000**, 95, S30-38.
5. Frank MM. Complement system, in Frank MM AK, Claman HN, Unanue ER, (eds): *Samter's Immunologic Diseases*. Boston, Little, Brown and Company. **1995**, 331-362.
6. Silva M. A brief survey of the history of inflammation. *Agents Action*. **1978**. 1994, 43, 86-90.
7. Ryan G.; Majno G. Acute inflammation. A review. *The American Journal of Pathology*. **1997**, 86 (1), 183-276.
8. Majno G. Chronic inflammation. *American Journal of Pathology*. **1998**, 153 (4), 1035-1039.
9. Guyton and Hall textbook of medical physiology.
10. Fakhoury M.; Negrulj R.; Mooranian A.; Al-Salami H. Inflammatory bowel disease: clinical aspects and treartment. *Journal of Inflammation Research*. **2014**, 7, 113-120.
11. Seyedian S.; Nokhostin.; Malamir M. A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. *Journal of Medicine and Life*. **2019**, 12 (2), 113-122.
12. Netter's anatomy flash cards 4th edition.

- 13.** Chen D.; Shen J.; Zhao W.; Wang T.; Han L.; Hamilton J.; Jeong H. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. *Bone Research*. **2017**, 5, 16044.
- 14.** Mandl. Osteoarthritis year in review 2018: clinical. *Osteoarthritis and Cartilage*. **2019**, 27 (3), 359-364.
- 15.** Asthma basic mechanisms and clinical management 3rd edition.
- 16.** Saha L. Irritable bowel syndrome: Pathogenesis, diagnosis, treatment, and evidence-based medicine. *World Journal of Gastroenterology*. **2014**, 20 (22), 6759-6773.
- 17.** Basnayake C. Treatment of irritable bowel syndrome. *Australian Prescriber*. **2018**, 41 (5), 145-149.
- 18.** Ganong's physiology examination and board review 1st edition.
- 19.** Quirt J.; Hikdebrand K.; Mazza J.; Noya F.; Kim H. Asthma. Allergy, *Asthma and Clinical immunology*. **2018**, 14 (2), 50.
- 20.** Text book of medical physiology 2nd edition.
- 21.** Ragab G.; Elshahaly M.; Badin T. Gout: An old disease in new perspective – A review. *Journal of Advanced Research*. **2017**, 8 (5), 495-511.
- 22.** Human Anatomy and Physiology 5th edition.
- 23.** Kelley and Firestein's Textbook of Rheumatology 10th edition.
- 24.** Smolen J S.; Aletaha D.; McInnes I B. Rheumatoid arthritis. *Lancet*. **2016**, 388 (10055), 2023-2038.
- 25.** Yelin E. Work disability in rheumatic diseases. *Curr Opin Rheumatol*. **2007**, 19 (2), 91-96.
- 26.** Boyle D.; Kim H.; Topolewski K.; Bartok B.; Firestein G. Novel Phosphoinositide 3-Kinase δ , γ Inhibitor: Potent Anti-Inflammatory Effects and Joint Protection in Models of Rheumatoid Arthritis. *J Pharmacol Exp Thera*. **2014**, 348, 271-280.

- 27.** Conigliaro P.; Triggianese P.; Martino E.; Chimenti M.; Sunzini F.; Viola A.; Claudia. Challenges in the treatment of Rheumatoid Arthritis. *Autoimmunity Reviews*. **2019**, 18, 706-713.
- 28.** Kaur K.; Kalra S.; Kaushak S. Systematic Review of Tofacitinib: A new Drug for the Management of Rheumatoid Arthritis. *Clinical Therapeutics*. **2014**, 36, 1074-1086.
- 29.** Jacqueline Bullock.; Syed A A.; Ayman M Saleh.; Sultan S Ahmed.; Duc p Do.; Rais A.; Ansari and Jasmin Ahmed. Rheumatoid Arthritis: A Brief Overview of the Treatment. *Med Princ Pract*. **2019**, 27 (6), 501-507.
- 30.** Sailliet N.; Brosseau C.; Robert J.; Brouard S. Role of JAK inhibitors and immune cells in transplantation. *Cytokine & Growth Factor Reviews*. **2019**, 47, 62-63.
- 31.** Hammaren H.; Virtanen A.; Raivola, J.; Silvennoinen O. The regulation of JAKs in cytokine signaling and its breakdown in disease. *Cytokine*. **2019**, 118, 48-63.
- 32.** Pellegrini S.; Dusanter-Fourt I. The structure, regulation and function of the Janus kinase (JAKs) and the signal transducers and activators of transcription (STATs). *Eur J Biochem*. **1997**, 15, 248 (3), 615-633.
- 33.** Vainchenker W.; Constantinescu S N. JAK/STAT signaling in hematological malignancies. *Oncogene*. **2013**, 32, 2601-2613.
- 34.** Kunihiro Yamaoka.; Pipsa Saharinen.; Marko Pesu.; Vance ET Holt III.; Olli Silvennoinen and John J O'Shea. The Janus kinase (Jaks). *Genome Biol*. **2004**, 5 (12), 253.
- 35.** Haan C.; Kreis S.; Mague C.; Behrmann I. Jaks and Cytokine receptors – An intimate relationship. *Biochemical Pharmacology*. **2006**, 72, 1538-1546.

- 36.** Elliott N.; Cleveland S.; Grann V.; Janik J.; Waldmann T.; Dave U. FERM domain mutations induce gain of function in JAK3 in adult T-Cell leukemia/lymphoma. *Bood.* **2011**, 118, 3911-3921.
- 37.** Becerra- Diaz M.; Valderrama-Carvakal H.; Terrazas L I. Signal Transducers and Activators of Transcription (STAT) Family Members in Helminth Infections. *International Journal of Biological Sciences.* **2011**, 7 (9), 1371-1381.
- 38.** Cheh Peng Lim.; Xinmin Cao. Structure, function, and regulation of STAT proteins. *Mol Biosyst.* **2006**, 2 (11), 536-550.
- 39.** Tracey J Mitchell and Susan John. Signal transducer and activator of transcription (STAT) signalling and T-cell lymphomas. *Immunology.* **2005**, 114 (3), 301-312.
- 40.** U Vinkemeier.; I Moarefi.; J E Darnell.; J Kuriyan. Structure of the amino-terminal protein interaction domain of STAT-4. *Science*, **1998**, 13, 279 (5353), 1048-1052.
- 41.** Ernest H Choy. Clinical significance of Janus Kinase inhibitor selectivity. *Rheumatology.* **2019**, 58, 6, 953-962.
- 42.** Chen M.; Cheng A.; Chen Y.; Hymel A.; Hanson E.; Kimmel L.; Minami Y.; Taniguchi T.; Changelian P.; John J. The amino terminus of JAK3 is necessary and sufficient for binding to the common γ Chain and confers the ability to transmit interleukin 2- mediated signals. *Immunology.* **1997**, 94, 6910-6915.
- 43.** Rhiannon Morris.; Nadia J Kershaw and Jeffrey J Babon. The molecular details of cytokine signaling via the JAK/STAT pathway. *Protein Sci.* **2018**, 27 (12), 1984-2009.
- 44.** Wei Wu and Xiao-Hong Sun. Janus kinase 3: the controller and controlled. *Acta Biochim Biophys Sin (Shanghai).* **2012**, 44 (3), 187-196.

- 45.** Thoma G.; Druckes P.; Zerwes H. Selective inhibitors of the Janus Kinase JAK3 - Are they effective? *Bioorg. Med. Chem. Lett.* **2014**, 24, 4617-4621.
- 46.** Flanagan M.; Blumenkopf T.; Brissette W.; Brown M.; Casavant j.; Shang-Poa C.; Doty J.; Elliott E.; Fisher M.; Hines M.; Kent C.; Kudlacz E.; Lillie B.; Magnuson K.; McCurdy, S.; Munchhof M.; Perry B.; Sawyer P.; Strelevitz T.; Subramanyam C.; Sun J.; Whipple D.; Changelian P. Discovery of CP-690,550: Apotent and selective Janus Kinase (JAK) inhibitor for the treatment of Autoimmune Diseases and Organ Transplant Rejection. *J. Med. Chem.* **2010**, 53, 8468-8484.
- 47.** Douglas.; Harrison. The JAK/STAT Pathway. *Cold Spring Harb Perspect Biol.* **2012**, 4 (3), a011205.
- 48.** Alejandro V Villarino.; Yuka Kanno and John J. O'Shea. Mechanism of Jak/STAT signaling in immunity and disease. *J. Immunol.* **2015**, 194 (1), 21-27.
- 49.** Kisseleva.; Bhattacharya S.; Braunstein J.; Schindler CW. Signaling through the JAK/STAT pathway, recent advances and future challenges. *Gene.* 285 (1-2), 1-24.
- 50.** Sigal L H. Basic Science for the clinician 41: tails of cytokine receptor activation and control: JAKs, STATs, PIASs, and SOCSs. *Clin Rheumatol.* **2006**, 12 (6), 315-9.
- 51.** Shuai K.; Liu B. Regulation of gene-activation pathways by PIAS proteins in the immune system. *Nat Rev Immunol.* **2005**, 5 (8), 593-605.
- 52.** Dan Xu and Cheng-Kui Qu. Protein tyrosine phosphatases in the JAK/STAT pathway. *Front Biosci.* **2008**, 13, 4925-4932.

- 53.** Ben A. Croker.; Hiu Kiu and Sandra E. Nicholson. SOCS Regulation of the JAK/STAT Signalling Pathway. *Semin Cell Dev Biol.* **2008**, 19 (4), 414-422.
- 54.** Lina Serhal.; Christopher J Edwards. Upadacitinib for the treatment of rheumatoid arthritis. *Expert Rev Clin Immunol.* **2019**, 15 (1), 13-25.
- 55.** Yoshiya Tanaka. A review of upadacitinib in rheumatoid arthritis. *Modern Rheumatology.* **2020**, 30 (5), 77-787.
- 56.** Kaur K.; Kalra S.; Kaushak S. Systematic Review of Tofacitinib: A new Drug for the Management of Rheumatoid Arthritis. *Clinical Therapeutics.* **2014**, 36, 1074-1086.
- 57.** Sohita Dhillon. Tofacitinib: A Review in Rheumatoid Arthritis. *Drugs.* **2017**, 77 (18), 1987-2001.
- 58.** Srdan Verstovsek. Ruxolitinib: An Oral Janus Kinase 1 and Janus Kinase 2 inhibitor in the Management of Myelofibrosis. *Postgrad Med.* **2013**, 125 (1), 128-135.
- 59.** John mascarenhas.; Ronald Hoffman. A comprehensive review and analsis of the effect of ruxolitinib therapy on the survival of patients with myelofibrosis. *Blood.* **2013**, 121 (24), 4832-4837.
- 60.** Harrison C.; Schaap N.; Vannucchi A.; Kiladjan J.; Tiu R.; Zachee P.; Jourdan E.; Winton E.; Silver R.; Schouten H.; Passamonti F.; Zweegman S.; Talpaz M.; Lager J.; Shun Z.; Mesa R. Janus kinase-2 inhibitor fedratinib in patients with myelofibrosis previously treated with ruxolitinib (JAKARTA-2): a single-arm, open-label, non-randomised, phase 2, multicentre study. *The Lancet haematology.* **2017**, 4, e317-e324.
- 61.** Ann Mullally.; John Hood.; Claire Harrison and Ruben Mesa. Fedratinib in myelofibrosis. *Blood Adv.* **2020**, 4 (8), 1792-1800.

- 62.** Sanchez G.; Reinhardt A.; Ramsey S.; Wittkowski H.; Hashkes P.; Berkun Y.; Schalm S.; Murias S.; Dare J.; Brown D.; Stone D.; Gao L.; Klausmeier T.; Foell D.; Jesus A.; Chapelle D.; Kim H.; Dill S.; Colbert R.; Failla L.; Kost B.; O'Brien M.; Reynolds J.; Folio L.; Calvo K.; Paul S.; Weir N.; Brofferio A.; Soldatos A.; Biancotto A.; Cowen E.; Digiovanna J.; Gadina M.; Lipton A.; Hadigan C.; Holland S.; Fontana J.; Alawad A.; Brown R.; Rother K.; Heller T.; Brooks K.; Kumar P.; Brooks S.; Waldman M.; Singh H.; Nickeleit V.; Silk M.; Prakash A.; Janes J.; Ozen S.; Wakim P.; Brogan P.; Macias W.; Goldbach-Mansky R. Jak1/2 inhibition with baricitinib in the treatment of autoinflammatory interferonopathies. *The Journal of Clinical Investigation*. **2018**, 28, 3041-3052.
- 63.** Al-Salama.; Scott L J. Baricitinib: A Review in Rheumatoid Arthritis. *Drugs*. **2018**. 78 (7), 761-772.
- 64.** Blunt M.; Koehrer S.; Dobson R.; Larrayoz M.; Wilmore S.; Hayman A.; Parnell J.; Smith L.; Davies A.; Johnson P.; Conley P.; Pandey A.; Strefford J.; Stevenson F.; Packham G.; Forconil F.; Coffey G.; Burger J.; Steele A. The dual syk/JAK inhibitor cerdulatinib antagonises B-cell receptor and microenvironment signaling in chronic lymphocytic leukemia. *Clin Cancer Res*. **2017**, 23, 2313-2324.
- 65.** Coffey G.; Betz A, DeGuzman F.; Pak Y.; Inagaki M.; Baker DC.; Hollenbach S J.; Pandey A.; Sinha U. The novel kinase inhibitor PRT062070 (Cerdulatinib) demonstrates efficacy in models of autoimmunity and - cell cancer. *The Journal of Pharmacology and Experimental Therapeutics*. **2014**, 351 (3), 538-548.
- 66.** J Berdeja.; F Palandri, M R Baer.; D. Quick.; J J Kiladjian.; G Martinelli.; A Verma.; O Hamid.; R Walgren C.; Pitou P.; T

- Gerds. Phase 2 study of gandotinib (LY2784544) in patients with myeloproliferative neoplasms. *Leukemia Research*. **2018**, 71, 82-88.
- 67.** Rami S Komrokji.; John F Seymour.; Andrew W Roberts.; Martha Wadleigh.; L Bik To.; Roby Scherber.; Elyce Turba.; Andrew Dorr.; Joy Zhu.; Lixia Wang.; Tnaya Granston.; Mary S. Campbell and Ruben A. Mesa. Results of a phase 2 study of pacritinib (SB1518), a JAK2/JAK2 (V617F) inhibitor, in patients with myelofibrosis. *Blood*. **2015**, 125 (17), 2649-2655.
- 68.** Genovese MC.; Westhovens R.; Meuleners L.; Van Der Aa A.; Harrison P.; Tasset C.; Kavanaugh A. Effect of Filgotinib, a selective JAK1 inhibitor, with or without Methotrexate in Patients with Rheumatoid Arthritis: Patient Reported Outcomes. *Arthritis Res Ther*. **2018**, 20 (1), 57.
- 69.** Martina Biggioggero.; Andrea Becciolini.; Chiara Crotti.; Elena Agape.; Ennio Giulio Favalli. Upadacitinib and filgotinib: the role of JAK1 selective inhibition in the treatment of rheumatoid arthritis. *Drugs Context*. **2019**, 8, 212595.
- 70.** Elizabeth O Hexner.; Cynthia Serdikoff.; Mahfuza Jan.; Cezary R Swider.; Candy Robinson.; Shi Yang.; Thelma Angeles.; Stephen G Emerson.; Martin Carroll.; Bruce Ruggeri.; Pawel Dobzanski. Lestaurtinib (CEP701) is a JAK2 inhibitor that suppresses JAK2/STAT5 signaling and the proliferation of primary erythroid cells from patients with myeloproliferative disorders. *Blood*. **2008**, 111 (12), 5663-5671.
- 71.** Massimo Gadina.; Daniella M Schwartz.; and John J O'Shea. Decertoinib: A Next-Generation Jakinib. *Arthritis rheumatol*. **2016**, 68 (10), 31-34.

- 72.** Harrison C.; Vannucchi A.; Platzbecker U.; Cervantes F.; Gupta, V.; Lavie D.; Passamonti F.; Winton E.; Dong H.; Kawashima J.; Maltzman J.; Kiladjian j.; Verstovsek S. Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial. *The Lancet haematology*. **2018**, 5, e73-e8.
- 73.** Palmer J.; Mesa R. The role of fedratinib for the treatment of patients with primary or secondary myelofibrosis. *Ther Adv Hemato.l* **2020**, 11, 1-7.
- 74.** Tefferi A.; Barracol D.; Lashol T.; Shah S.; Begna K. H.; Kali A.; HoganW.; Litzow M.; Hanson C.; Ketterling R.; Gangat N.; Pardananni A. Momelotinib therapy for myelofibrosis: a 7-year follow up. *Blood Cancer Journal*. **2018**, 8-29.
- 75.** Ma J.; Xing W.; Coffey G.; Dresser K.; Lu K.; Guo A.; Raca G.; Pandey A.; Conley P.; Yu H.; Wang Y. Cerdulatinib, a novel dual SYK/JAK kinase inhibitor, has broad anti-tumor activity in both ABC and GCB types of diffuse large B cell lymphoma. *Oncotarget*. **2015**, 22, 6 (41), 43881-43896.
- 76.** Paulsen J.; Liu J.; Bolstad D.; Smith A.; Priesley N.; Wright D.; Anderson A. In vitro biological activity and structural analysis of 2, 4-diamino-5-(20-arylpropargyl)pyrimidine inhibitors of *Candida albicans*. *Bioorganic & Medicinal Chemistry*. **2009**, 17, 4866 – 4872.
- 77.** Phuangsawai O.; Beswick P.; Ratanabunyong S.; Tabtimmai L.; Suphakun P.; Obounchoey P.; Hannongbua S.; Ward S.; Choowongkamon K and Gleeson M. Evaluation of the anti-malarial activity and cytotoxicity of 2,4-diamino pyrimidine-based kinase inhibitors. *European Journal of Medicinal Chemistry*. **2016**, 124, 896 – 905.

- 78.** Achary R.; Mathi G R.; Lee D H.; Yun C S.; Lee C O.; Kim H R.; Park C H.; Kim P and Hwang J. Novel 2,4-diaminopyrimidines bearing fused tricyclic ring moiety for anaplastic lymphoma kinase (ALK) inhibitor. *Bioorganic & Medicinal Chemistry Letters*. **2017**, 27, 2185 – 2191.
- 79.** Powell N.; Hoffman J.; Ciske F.; Kaufman M.; Kohrt J.; Quin J.; Sheehan D.; Delaney A.; Baxi S.; Catana C.; McConnell.; Ohren J.; Perrin L.; Edmunds J. Highly selective 2,4-diaminopyrimidine-5-carboxamide inhibitors of Sky kinase. *Bioorganic & Medicinal Chemistry Letters*. **2013**, 23, 1046 – 1050.
- 80.** Jahangir A.; Alam M.; Carter D.; Dillon M.; Bois D.; Ford A.; Gever J.; Lin C.; Wagner P.; Zhai Y.; Zira J. Identification and SAR of novel diaminopyrimidines. Part 2: The discovery of RO-51, a potent and selective, dual P2X₃/P2X_{2/3} antagonist for the treatment of pain. *Bioorganic & Medicinal Chemistry Letters* **2009**, 19, 1632 – 1635.
- 81.** Patel S.; Modi P.; Ranjan V.; Chhabria M. Structure-based design, synthesis and evaluation of 2,4-diaminopyrimidine derivatives as novel caspase-1 inhibitors. *Bioorganic Chemistry*, **2018**, 78, 258 – 268.
- 82.** Hockov D.; Holy A.; Masojidkova M.; Andrei G.; Snoeck R.; Clercq E D and Balzarini J. Synthesis and antiviral activity of 2,4-diamino-5-cyano-6- [2-(phosphonomethoxy)ethoxy]pyrimidine and related compounds. *Bioorganic & Medicinal Chemistry*, **2004**, 12, 3197 – 3202.
- 83.** Nishiwaki N.; Ogihara T.; Takami T.; Tamura M and Ariga M. New Synthetic Equivalent of Nitromalonaldehyde Treatable in Organic Media. *Journal of Organic Chemistry*. **2004**, 69, 24, 8382 – 8386.

- 84.** Li X.; Tang G.; Wang Y.; Zhou Y.; Wang X.; Guo T.; Xia M.; Ding N and Pan Z. Discovery of a Series of 2,5-Diaminopyrimidine Covalent Irreversible Inhibitors of Bruton's Tyrosine Kinase with in Vivo Antitumor Activity. *Journal of Medicinal Chemistry*, **2014**, 57, 12, 5112 – 5128.
- 85.** Grossmann.; Andre and Krahwinkel. Process for preperation of 4,6-dihydroxypyrimidine. PCT Int. Appl., **2020**, 2020136130.
- 86.** Zhang S.; Zhang W.; Xiao Q.; Yang Z.; Hu X.; Wei Z and Tam K. Development of dichloroacetamide pyrimidines as pyruvate dehydrogenase kinase inhibitors to reduce cancer cell growth: synthesis and biological evaluation. *RSC Advances*, **2016**, 82.
- 87.** Bendich A.; Russell P.; Fox J. The Synthesis and Properties of 6-Chlor.; opurine and Purine. *Journal of American Chemical Society*. **1954**, 76, 23, 6073 – 6077.
- 88.** Koziakov D.; Majek M.; Wangelin A. Metal-free radical thiolations mediated by very weak bases. *Organic and Biomolecular Chemistry*. **2016**, 14 (48), 11347-11352.
- 89.** Walker D P.; Zawistoski M P.; McGlynn M A.; Li J C.; Kung D W.; Bonnette P C.; Baumann A.; Buckbinder L.; Houser J A.; Boer J.; Mistry A.; Han S.; Xing L.; Guzman-Perez A. Sulfoximine-substituted trifluoromrthylpyrimidine analogs as inhibitors of proline-rich tyrosine kinase 2 (PYK2) show reduce hERG activity. *Bioorganic and Medicinal Chemistry Letters*. **2009**, 19 (12), 3253-3258.
- 90.** Hayashi N.; Sato K.; Sato Y.; Iwagami M.; Nishimura M.; Yashino J.; Higuchi H.; Sato T. Elongation of phenoxide C-O bonds due to formation of multifold hydrogen bonds: statistical, experimental, and theoretical studies. *Journal of Organic Chemistry*. **2011**, 76 (14), 5747-5758.

- 91.** Thombare P.; Argade A.; Jain M.; Gite S. Heterocyclic Compounds. WO 2013/054351 A1.
- 92.** Malerich J.; Lam J.; Hart B.; Fine R.; Klebansky B.; Tanga M.; D'Andrea A.; Diamino 1,2,4-triazole derivatives are selective inhibitors of TYK2 and JAK1 over JAK2 and JAK3, *Bioorganic and Medicinal Chemistry letters*. **2010**, 20, 7454–7457.
- 93.** Ozcan S.; Kazi A.; Marsilio F.; Fang B.; Guida W C.; Koomen J.; Lawewnce H R.; Sebti S. Oxadiazole-isopropylamides as Potent and Noncovalent Proteasome Inhibitors. *Journal of Medicinal Chemistry*. **2013**. 56 (10), 3783-3805.
- 94.** Enderes G W.; Lee P H.; Olson K L.; Kramer J B.; Ciske F L.; Barretett S D. Multi hetroaryl compounds as inhibitors of H-PGDS and their use for treating prostaglandin D2 mediated diseases. WO/2010/033977.
- 95.** Lin T.; Quadros H. E.; Nickerson-Nutter C.; Appell K.; Cole A.; Shao Y.; Tam S.; Ohlmeyer M.; Wang B.; Goodwin D.; Kimble E.; Quintero J.; Gao M.; Symanowicz P.; Wrocklage C.; Lussier J.; Schelling S.; Hewet A.; Xuan D.; Krykbaev R.; Togias J.; Xu X.; Harrison R.; Mansour T.; Collins M.; Clark J.; Webb M.; Seidl K. Selective functional inhibition of JAK3 is sufficient for efficacy in collagen-induced arthritis in mice. *Arthritis Rheum*. **2010**, 62, 2283-2293.
- 96.** Botta A.; Sirignano E.; Popolo A.; Saturnino C.; Terracciano S.; Foglia A.; Sinicroppi M.; Longo P.; Micco S. Identification of lead compounds as inhibitors of STAT3: design, synthesis and bioactivity, *Mol. Inform*. **2015**, 34, 689-697.
- 97.** Soth M.; Hermann J C.; Yee C.; Alam M.; Barnett J W.; Berry P.; Browner M F.; Frank K.; Frauchiger S.; Harris S.; He Y.; Hekmat-Nejad M.; Hendricks T.; Henningsen R.; Hilgenkamp R.;

- HO H.; Hoffman A.; Hsu P.; Hu D.; Itano A.; Jaime-Figueraoa S.; Jahangir A.; Jin S.; Kuglstatter A.; Kutach A.; Liao C.; Lynch S.; Menke J.; Niu L.; Patel V.; Railkar A.; Roy D.; Shao A.; Shaw D.; Steiner S.; Sun Y.; Tan S.; Wang S.; Vu M D. 3-Amido Pyrrolopyrazine JAK Kinase Inhibitors: Development of a JAK3 vs Selective Inhibitor and Evaluation in Cellular and in Vivo Models. *Jornal of Medicinal Chemistry*. **2013**, 56, 345-356.
- 98.** Kumar G N.; Surapaneni S. Role of Drug Metabolism in Drug Discovery and Development. *Medicinal Research Reviews*. **2001**, 21 (5), 397-411.
- 99.** Jin F.; Robeson F.; Zhou H.; Moyer C.; Wilbert S.; Murray B.; Ramanathan S. Clinical drug interaction profile of idelalisib in healthy subjects. *The journal of clinical pharmacology*. **2015**, 55, 909-919.
- 100.** Nakajima Y.; Inoue T.; Nakai K.; Mukoyoshi K.; Hamaguchi H.; Hatanaka K.; Sasaki H.; Tanaka A.; Takahashi F.; Kunikawa S.; Usuda H.; Moritimo A.; Higashi Y.; Inami M.; Shirakami S. Synthesis and evaluation of novel 1H-pyrrolo[2,3-b]pyridine-5-carboxamide derivatives as potent and orally efficacious immunomodulators targeting JAK3. *Bioorganic and Medicinal Chemistry*. **2015**, 23, 4871-4883.
- 101.** Flanagan M E.; Blumenkopf T A.; Brissette W H.; Brown M F.; Casavant J M.; Shang-Poa C.; Doty J L.; Elliott E A.; Fisher M B.; Hines M.; Kent C.; Kudlacz E M.; Lillie B M.; Magnuson K S.; McCurdy S P.; Munchhof M J.; Perry B D.; Sawyer P S.; Strelevitz T J.; Chakrapani S.; Sun J.; Whipplw D A.; Changelianr P S. Discovery of CP-690,550: A Potent and Selective Janus Kinase (JAK) Inhibitor for the Treatment of

- Autoimmune Diseases and Organ Transplant Rejection. *Journal of Medicinal Chemistry*. **2010**, 53, 8468-8484.
- 102.** Qian M.; Bai S.; Brogdon B.; Wu J.; Liu R.; Civingston M.; Vaddi K.; Newton R.; Fossler M.; Garner E.; Deng Y.; Maduskuie T.; Trzaskos J.; Duan J.; Deccicco C.; Christ D. Pharmacokinetics and Pharmacodynamics of DPC 333 ((2R)-2-((3R)-3-Amino-3{4-[2-methyl-4-quinoliny) methoxy] phenyl}-2-oxopyrrolidinyI)-N-hydroxy-4-methylpentanamide)), a Potent and Selective inhibitor, of Tumor necrosis Factor α -Converting Enzyme in Rodents, Dogs, Chimpanzees, and Humans. *Drug metabolism and disposition*. **2007**, 335, 1916-1925.
- 103.** Bevaart L.; Vervoordeldonk M.; Tak P. Evaluation of therapeutic targets in animal models of arthritis: How does it relate to rheumatoid arthritis? *Arthritis Rheum*. **2010**, 62, 2192-2205.
- 104.** Zhao Y.; Liu Y.; Zhou D.; Dai Q.; Liu S. Anti-arthritic effect of chebulanin on collagen-induced arthritis in mice. *PLoS ONE*. **2015**, 1-14.
- 105.** Yamazaki K.; Aiso S.; Matsumoto M.; Arito H.; nagano K.; Yamamoto S.; Matsushima T. Thirteen-Week Oral Toxicity study of 1, 4-Dichloro-2-Nitrobenzene in Rats and Mice. *Industrial Health*. **2005**, 43, 598-610.
- 106.** Berman H.; Westbrook J.; Feng Z.; Gililand G.; Bhat T.; Weissing H.; Shindyalov I.; Bourne P. The Protein Data Bank. *Nucleic Acid Research*. **2000**, 28, 235-242.
- 107.** Schrodinger Release, 2018-3: Glide, Schrodinger, LLC, New York, NY, **2018**.