

Chapter 6

References

- Abdelilah S, Latifa K, Esra N, Cameron L, Bouchaib L, Nicolaides N, Levitt R, Hamid Q. Functional expression of IL-9 receptor by human neutrophils from asthmatic donors: role in IL-8 release. *J Immunol.* 2001; 166: 2768-2774.
- Abdel-Latif D, Steward M, Macdonald DL, Francis GA, Dinauer MC, Lacy P. Rac2 is critical for neutrophil primary granule exocytosis. *Blood.* 2004; 104: 832-839.
- Adkinson AF Jr, Yunginger JW, Busse WW, Bochner BS, Holgate S, Simons FE. Biology of Neutrophils. *Middleton's Allergy Principles & Practice.* 2003; 291;
- Akgul C, Edwards SW. Regulation of neutrophil apoptosis via death receptors. *Cell Mol Life Sci.* 2003; 60: 2402-2408.
- Akman A, Irkeç M, Orhan M. Effects of Iodoxamide, disodium cromoglycate and fluorometholone on tear leukotriene levels in vernal keratoconjunctivitis. *Eye (Lond).* 1998; 12: 291-295.
- Al Omari MM, Zoubi RM, Hasan El, Khader TZ, Badwan AA. Effect of light and heat on the stability of montelukast in solution and in its solid state. *J Pharm Biomed Anal.* 2007; 45: 465-471.
- Ali H, Sozzani S, Fisher I, Barr AJ, Richardson RM, Haribabu B, Snyderman R. Differential regulation of formyl peptide and platelet-activating factor receptors: role of phospholipase C β 3 phosphorylation by protein kinase A. *J Biol Chem.* 1998; 273: 11012–11016.
- Anderson R, Goolam Mahomed A, Theron AJ, Ramafi G, Feldman C. Effects of rolipram and dibutyryl cyclic AMP on resequestration of cytosolic calcium in FMLP-activated human neutrophils. *Br J Pharmacol.* 1998; 124: 547–555.
- Anderson R, Steel HC, Tintinger GR. Inositol 1,4,5-triphosphate-mediated shuttling between intracellular stores and the cytosol contributes to the sustained elevation in

cytosolic calcium in FMLP-activated human neutrophils. *Biochem Pharmacol.* 2005; 69: 1567-1575.

Anderson R, Theron AJ, Gravett CM, et al. Montelukast inhibits neutrophil pro-inflammatory activity by a cyclic AMP-dependent mechanism. *Br J Pharmacol.* 2009; 156: 105–115.

Anderson R, Visser SS, Ramafi G, Theron AJ. Accelerated resequestration of cytosolic calcium and suppression of the proinflammatory activities of human neutrophils by CGS 21680. *Br J Pharmacol.* 2000; 130: 717–724.

Andina N, Conus S, Schneider EM, Fey MF, Simon HU. Induction of Bim limits cytokine-mediated prolonged survival of neutrophils. *Cell Death Differ.* 2009; 16: 1248-1255.

Anonymous. Drug Review. Asthma. Montelukast, drugs in context. Part E. *Respir Med.* 2004; Infect 1: 1–40.

Bacharier LB, Boner A, Carlsen KH, et al. Diagnosis and treatment of asthma in childhood: a PRACTALL consensus report. *Allergy.* 2008; 63: 5-34.

Bai Y, Sanderson MJ. Airway smooth muscle relaxation results from a reduction in the frequency of Ca^{2+} oscillations induced by a cAMP-mediated inhibition of the IP₃ receptor. *Respir Res.* 2006; 7: 34.

Bai Y, Sanderson MJ. Airway smooth muscle relaxation results from a reduction in the frequency of Ca^{2+} oscillations induced by a cAMP-mediated inhibition of the IP₃ receptor. *Respir Res.* 2006; 7: 34

Baldridge, C. W., Gerard, R. W. The extra respiration of phagocytosis. *Am. J. Physiol.* 1933; 103: 235-236

Babior BM, Lambeth JD, Nauseef W. The Neutrophil NADPH Oxidase. Review. *Arch Biochem Biophys.* 2002; 397: 342-344.

Barkhof F, Hulst HE, Drulovic J, Uitdehaag BM, Matsuda K, Landin R. Ibdilast in relapsing-remitting multiple sclerosis: a neuroprotectant? *Neurology.* 2010; 74: 1033-1040.

Barnes PJ. New molecular targets for the treatment of neutrophilic diseases. *J Allergy Clin Immunol.* 2007; 119: 1055–1062.

Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, Gibson P, Ohta K, O'Byrne P, Pedersen SE, Pizzichini E, Sullivan SD, Wenzel SE, Zar HJ. Global strategy for asthma management and prevention: GINA executive summary.

Eur Respir J. 2008; 31: 143-178

Bautz F, Denzlinger C, Kanz L, Möhle R. Chemotaxis and transendothelial migration of CD34+ hematopoietic progenitor cells induced by the inflammatory mediator leukotriene D4 are mediated by the 7-transmembrane receptor CysLT1. *Blood.* 2001; 97: 3433–3440.

Beatty K, Robertie P, Senior RM, Travis J. Determination of oxidized alpha-1-proteinase inhibitor in serum. *J Lab Clin Med.* 1982; 100: 186–192.

Bengis-Garber C, Gruener N. Protein kinase A downregulates the phosphorylation of p47 phox in human neutrophils: a possible pathway for inhibition of the respiratory burst. *Cell Signal.* 1996; 8: 291–296.

Binnaz A, Iyanoye A, Sieck G, Prakash YS, Pabelick CM. Cyclic nucleotide regulation of store-operated Ca²⁺ influx in airway smooth muscle. *Am J Physiol Lung Cell Mol Physiol.* 2006; 290: L278–L283.

Bisgaard H. A randomized trial of montelukast in respiratory syncytial virus postbronchiolitis. *Am J Respir Crit Care Med.* 2003; 167: 379–383.

Borgeat P, Samuelsson B. Arachidonic acid metabolism in polymorphonuclear leukocytes: unstable intermediate in formation of dihydroxy acid. *Proc Natl Acad Sci USA.* 1979(a); 79: 3213-3217.

Borgeat P, Samuelsson B. Metabolism of arachidonic acid in polymorphonuclear leukocytes. Structural analysis of novel hydroxylated compounds. *J Biol Chem.* 1979(b); 254: 7865-7869.

Borgeat P, Samuelsson B. Transformation of arachidonic acid by rabbit polymorphonuclear leukocytes. Formation of a novel dihydroxyeicosatetraenoic acid. *J Biol Chem.* 1979(c); 254: 2643-2646.

Borregaard N, Sørensen OE, Theilgaard-Mönch K. Neutrophil granules: a library of innate immunity proteins. *Trends Immunol.* 2007; 28: 340-345.

Borregaard N. Subcellular localization and dynamics of components of the respiratory burst oxidase. *J Bioenerg Biomembr.* 1988; 20: 637-651.

Bouin AP, Grandvaux N, Vignais PV, Fuchs A. p40(phox) is phosphorylated on threonine 154 and serine 315 during activation of the phagocyte NADPH oxidase. Implication of a protein kinase c-type kinase in the phosphorylation process. *J Biol Chem.* 1998; 273: 30097-30103.

Bousquet J, Boulet LP, Peters MJ, Magnussen H, Quiralte J, Martinez-Aguilar NE, Carlsheimer A. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. *Respir Med.* 2007; 101: 2437- 2446.

Bowers RC, Hevko J, Henson PM, Murphy RC. A novel glutathione containing eicosanoid (FOG7) chemotactic for human granulocytes. *J Biol Chem.* 2000; 275: 29931-29934.

Bréchard S, Melchior C, Plançon S, Schenten V, Tscherhart EJ. Store-operated Ca^{2+} channels formed by TRPC1, TRPC6 and Orai1 and non-store-operated channels formed by TRPC3 are involved in the regulation of NADPH oxidase in HL-60 granulocytes. *Cell Calcium.* 2008; 44: 492-506.

Bréchard S, Tscherhart EJ. Regulation of superoxide production in neutrophils: role of calcium influx. *J Leuk Biol.* 2008; 84: 1–15.

Brink C, Dahlén SE, Drazen J, Evans JF, Hay DW, Rovati GE, Serhan CN, Shimizu T, Yokomizo T. International Union of Pharmacology XLIV. Nomenclature for the oxoeicosanoid receptor. *Pharmacol Rev.* 2004; 56: 149-157.

Brocklehurst WE. The release of histamine and formation of slow reacting substance (SRS-A) during anaphylactic shock. *J Physiol.* (London). 1960; 151: 416-435

Brown GE, Stewart MQ, Liu H, Ha VL, Yaffe MB. A novel assay system implicates PtdIns(3,4)P(2), PtdIns(3)P, and PKC delta in intracellular production of reactive oxygen species by the NADPH oxidase. *Mol Cell.* 2003; 11: 35-47.

Burelout C, Thibault N, Harbour D, Naccache PH, Bourgoin SG. The PGE2-induced inhibition of the PLD activation pathway stimulated by fMLP in human neutrophils is mediated by PKA at the PI3-Kgamma level. *Biochem Pharmacol.* 2007; 74: 730–741.

Burns AR, Walker DC, Brown ES, Thurmon LT, Bowden RA, Keese CR, Simon SI, Entman ML, Smith CW. Neutrophil transendothelial migration is independent of tight

junctions and occurs preferentially at tricellular corners. *J Immunol.* 1997; 159: 2893-2903.

Cadwallader KA, Condliffe AM, McGregor A, et al. Regulation of phosphatidylinositol 3-kinase activity and phosphatidylinositol 3,4,5-trisphosphate accumulation by neutrophil priming agents. *J Immunol.* 2002; 169: 3336-3344.

Cai TQ, Wright SD. Human leukocyte elastase is an endogenous ligand for the integrin CR3 (CD11b/CD18, Mac-1, alpha M beta 2) and modulates polymorphonuclear leukocyte adhesion. *J Exp Med.* 1996; 184: 1213-1223.

Campbell EJ, Campbell MA, Owen CA. Bioactive proteinase 3 on the cell surface of human neutrophils: quantification, catalytic activity, and susceptibility to inhibition. *J Immunol.* 2000; 165: 3366-3374.

Capra V, Ambrosio M, Riccioni G, et al. Cysteinyl-leukotriene receptor antagonists: present situation and future opportunities. *Curr Med Chem.* 2006; 13: 3213–3216.

Capra V. Molecular and functional aspects of human cysteinyl leukotriene receptors. *Pharmacol Res.* 2004; 50: 1-11.

Carroll N, Carello S, Cooke C, James A. Airway structure and inflammatory cells in fatal attacks of asthma. *Eur Respir J.* 1996; 9: 709-715.

Cauwe B, Opdenakker G. Intracellular substrate cleavage: a novel dimension in the biochemistry, biology and pathology of matrix metalloproteinases. *Crit Rev Biochem Mol Biol.* 2010; 45 :351-423.

Celik P, Sakar A, Havlucu Y, Yuksel H, Turkdogan P, Yorganioglu A. Short-term effects of montelukast in stable patients with moderate to severe COPD. *Respir Med.* 2005; 99: 444–450.

- Cheng H, Leff JA, Amin R, Gertz BJ, De Smet M, Noonan N, Rogers JD, Malbecq W, Meisner D, Somers G. Pharmacokinetics, bioavailability, and safety of montelukast sodium (MK-0476) in healthy males and females. *Pharm Res*. 1996; 13: 445–448.
- Cheng H, Leff JA, Amin R, Gertz BJ, De Smet M, Noonan N, Rogers JD, Malbecq W, Meisner D, Somers G. Pharmacokinetics, bioavailability, and safety of montelukast sodium (MK-0476) in healthy males and females. *Pharm Res*. 1996; 13: 445–448.
- Chessa TA, Anderson KE, Hu Y, Xu Q, Rausch O, Stephens LR, Hawkins PT. Phosphorylation of threonine 154 in p40phox is an important physiological signal for activation of the neutrophil NADPH oxidase. *Blood*. 2010; 116: 6027-6036.
- Chu G, Lester JW, Young KB, Luo W, Zhai J, Kranias EG. A single site (Ser16) phosphorylation in phospholamban is sufficient in mediating its maximal cardiac responses to beta-agonists. *J Biol Chem*. 2000; 275: 38938–38943.
- Ciana P, Fumagalli M, Trincavelli ML, et al. The orphan receptor GPR17 identified as a new dual uracil nucleotides/cysteinyl-leukotrienes receptor. *EMBO J*. 2006; 25: 4615-1627.
- Coffey MJ, Phare SM, Peters-Golden M. Prolonged exposure to lipopolysaccharide inhibits macrophage 5-lipoxygenase metabolism via induction of nitric oxide synthesis. *J Immunol*. 2000; 165: 3592-3598.
- Collins SR, Meyer T. Evolutionary origins of STIM1 and STIM2 within ancient Ca^{2+} signalling systems. *Trends Cell Biol*. 2011; 21: 202-211.
- Condliffe A. M, P T. Hawkins L R. Stephens C. Haslett E R. Chilvers. Priming of human neutrophil superoxide generation by tumour necrosis factor- α is signalled by

- enhanced phosphatidylinositol 3,4,5-trisphosphate but not inositol 1,4,5-trisphosphate accumulation. *FEBS Lett.* 1998; 439: 147.
- Condliffe AM, Davidson K, Anderson KE, Ellson CD, Crabbe T, Okkenhaug K, Vanhaesebroeck B, Turner M, Webb L, Wymann MP, Hirsch E, Ruckle T, Camps M, Rommel C, Jackson SP, Chilvers ER, Stephens LR, Hawkins PT. Sequential activation of class IB and class IA PI3K is important for the primed respiratory burst of human but not murine neutrophils. *Blood*. 2005; 106: 1432-1440.
- Corren J, Lemanske RF, Hanania NA, Korenblat PE, Parsey MV, Arron JR, Harris JM, Scheerens H, Wu LC, Su Z, Mosesova S, Eisner MD, Bohen SP, Matthews JG. Lebrikizumab treatment in adults with asthma. *N Engl J Med*. 2011;365: 1088-1098.
- Coskun AK, Yigiter M, Oral A, Odabasoglu F, Halici Z, Mentes O, Cadirci E, Atalay F, Suleyman H. The effects of montelukast on antioxidant enzymes and proinflammatory cytokines on the heart, liver, lungs, and kidneys in a rat model of cecal ligation and puncture-induced sepsis. *ScientificWorldJournal*. 2011; 11: 1341-56.
- Cosmi L, Liotta F, Maggi E, Romagnani S, Annunziato F. Th17 cells: new players in asthma pathogenesis. *Allergy*. 2011; 66: 989-998.
- Cowan DC, Cowan JO, Palmary R, Williamson A, Taylor DR. Heterogeneity of asthma according to blood inflammatory patterns. *Thorax*. 2009; 64: 374-380.
- Currie GP, Lee DKC, Dempsey OJ, Fowler SJ, Cowan LM, Lipworth BJ. A proof of concept study to evaluate putative benefits of montelukast in moderate persistent asthmatics. *Br J Clin Pharmacol*. 2003; 55: 609–615.

- Currie GP, McLaughlin K. The expanding role of leukotriene receptor antagonists in chronic asthma. *Ann Allergy Asthma Immunol.* 2006; 97: 731-741.
- Currie GP, Srivastava P, Dempsey OJ, Lee DKC. Therapeutic modulation of allergic airways disease with leukotriene receptor antagonists. *Q J Med.* 2005; 98: 171–182.
- Czermak BJ, Lentsch AB, Bless NM, Schmal H, Friedl HP, Ward PA. Role of complement in in vitro and in vivo lung inflammatory reactions. *J Leukoc Biol.* 1998; 64: 40-48.
- Dal Negro RW, Borderias L, Zhang Q, Fan T, Sazonov V, Guilera M, Taylor SD. Rates of asthma attacks in patients with previously inadequately controlled mild asthma treated in clinical practice with combination drug therapy: an exploratory post-hoc analysis. *BMC Pulm Med.* 2009; 9:10.
- Dang PM, Stensballe A, Boussetta T, Dewas H, Kroviarski Y, Hayem G, Jensen ON, Gougerot-Pocidalo MA, El-Benna J. A specific P47phox serine phosphorylated by convergent MAPKs mediates neutrophil NADPH oxidase priming at inflammatory sites. *J Clin Invest.* 2006; 116: 2033–2043.
- Daniele S, Trincavelli ML, Gabelloni P, Lecca D, Rosa P, Abbracchio MP, Martini C. Agonist-Induced Desensitization/Resensitization of Human G Protein-Coupled Receptor 17: A Functional Cross-Talk between Purinergic and Cysteinyl-Leukotriene Ligands. *J Pharmacol Exp Ther.* 2011; 338: 559-567.
- Dempsey OJ, Wilson Am, Sims Ej, Mistry C, Lipworth BJ. Additive bronchoprotective and bronchodilator effects with doses of salmeterol and montelukast in asthmatic patients receiving inhaled corticosteroids. *Chest.* 2000; 117: 950-953.

Devchand PR, Keller H, Peters JM, Vazquez M, Gonzalez FJ, Wahli W. The PPARalpha-leukotriene B4 pathway to inflammation control. *Nature*. 1996; 384: 39-43.

Dewas C, Dang PM, Gougerot-Pocidalo MA, El-Benna J. TNF-alpha induces phosphorylation of p47(phox) in human neutrophils: partial phosphorylation of p47phox is a common event of priming of human neutrophils by TNF-alpha and granulocyte-macrophage colony-stimulating factor. *J Immunol*. 2003; 171: 4392-4398.

Deykin A, Wechsler ME, Boushey HA, Chinchilli VM, Kinselman SJ, Craig TJ, DiMango E, Fahy JV, Kraft M, Leone F, Lazarus SC, Lemanske RF Jr, Martin RJ, Pesola GR, Peters SP, Sorkness CA, Szeffler SJ, Israel E. Combination therapy with a long-acting beta-agonist and a leukotriene antagonist in moderate asthma. *Am J Respir Crit Care Med*. 2007; 175: 228-234.

Diamant Z, van der Molen T. Treating asthma: is there a place for leukotriene receptor antagonists? *Respir Med*. 2005; 99: 655–662.

Doerschuk CM, Beyers N, Coxson HO, Wiggs B, Hogg JC. Comparison of neutrophil and capillary diameters and their relation to neutrophil sequestration in the lung. *J Appl Physiol*. 1993; 74: 3040-3045.

Doerschuk CM, Tasaka S, Wang CD11/CD18-dependent and -independent neutrophil emigration in the lungs: how do neutrophils know which route to take? *Am J Respir Cell Mol Biol*. 2000; 23: 133-136.

Drakatos P, Lykouras D, Sampsonas F, Karkoulas K, Spiropoulos K. Targeting leukotrienes for the treatment of COPD? *Inflamm Allergy Drug Targets*. 2009; 8: 297-306.

Dupont L, Potvin E, Korn A, Lachman M, Gusman J, Pechè R. Improving asthma in patients suboptimally controlled on inhaled steroids and long-acting beta₂-agonists: addition of montelukast in an open-label pilot study. *Curr Med Res Opin*. 2005; 21: 863-869.

Duroudier NP, Tulah AS, Sayers I. Leukotriene pathway genetics and pharmacogenetics in allergy. *Allergy*. 2009; 64: 823-839.

Durrani SR, Viswanathan RK, Busse WW. What effect does asthma treatment have on airway remodeling? Current perspectives. *J Allergy Clin Immunol*. 2011; 128: 439-448.

Ehlers MR. CR3: a general purpose adhesion-recognition receptor essential for innate immunity. *Microbes Infect*. 2000; 2: 289-294.

Farr SJ, Rowe AM, Rubsamen R, et al. Aerosol deposition in the human lung following administration from a microprocessor controlled pressurized metered dose inhaler. *Thorax*. 1995; 50: 639–644.

Feldberg W and Kellaway CW. Liberation of histamine and formation of lysocithin-like substance by cobra venom. *J Physiol*. (London). 1938; 94: 187-226.

Ferrari F, Mennuni L, Caselli G, Zanelli T, Makovec F. Pharmacological profile of CR3465, a new leukotriene CysLT1 receptor antagonist with broad anti-inflammatory activity. *Eur J Pharmacol*. 2004; 504: 223-233.

Feske S, Gwack Y, Prakriya M, Srikanth S, Poppel SH, Tanasa B, Hogan PG, Lewis RS, Daly M, Rao A. A mutation in Orai1 causes immune deficiency by abrogating CRAC channel function. *Nature*. 2006; 441: 179-185.

Field SK. Roflumilast: an oral, once-daily selective PDE-4 inhibitor for the management of COPD and asthma. *Expert Opin Investig Drugs*. 2008; 17: 811-818.

Flamand N, Surette ME, Picard S, Bourgoin S, Borgeat P. Cyclic AMP-mediated inhibition of 5-lipoxygenase translocation and leukotriene biosynthesis in human neutrophils. *Mol Pharmacol*. 2002; 62: 250–256.

Fleisch JH, Rinkema LE, Marshall WS. Pharmacologic receptors for the leukotrienes. *Biochem Pharmacol*. 1984; 33: 3919-3922.

Fligiel SE, Standiford T, Fligiel HM, Tashkin D, Strieter RM, Warner RL, Johnson KJ, Varani J. Matrix metalloproteinases and matrix metalloproteinase inhibitors in acute lung injury. *Hum Pathol*. 2006; 37: 422-430.

Folko G, Murphy RC. Eicosanoid transcellular biosynthesis: from cell-cell interaction to in vivo tissue responses. *Pharmacol Rev*. 2006; 58: 375-388

Fox S, Leitch AE, Duffin R, Haslett C, Rossi AG. Neutrophil apoptosis: relevance to the innate immune response and inflammatory disease. *J Innate Immun*. 2010; 2: 216-227.

Fox-Spencer R. Drug review. Allergic rhinitis and asthma. Montelukast. *Drugs Context*. 2006; 2: 413–456.

Fregonese L, Stolk J. Hereditary alpha-1-antitrypsin deficiency and its clinical consequences. *Orphanet J Rare Dis*. 2008; 3: 16.

Frey RS, Ushio-Fukai M, Malik AB. NADPH oxidase-dependent signaling in endothelial cells: role in physiology and pathophysiology. *Antioxid Redox Signal*. 2009; 11: 791-810.

Friedlander AL, Albert RK. Chronic macrolide therapy in inflammatory airways diseases. *Chest*. 2010; 138: 1202-12.

Fukuda M, Suzuki Y, Hino H, Morimoto T, Ishii E. Activation of central adenosine (2A) receptors lowers the seizure threshold of hyperthermia-induced seizure in childhood rats. *Seizure*. 2011; 20: 156-159.

Gane J, Stockley R. Mechanisms of neutrophil transmigration across the vascular endothelium in COPD. *Thorax*. 2011; 10: 1136.

Gay JC. Priming of neutrophil oxidative responses by platelet-activating factor. *J Lipid Mediat*. 1990; 2 Suppl: S161-S175.

Geiszt M, Kapus A, Nemet K, Farkas L, Ligeti F. Regulation of capacitative calcium influx in neutrophil granulocytes: alterations in chronic granulomatous disease. *J Biol Chem*. 1997; 272: 26471–26478.

Gelfand EW, Dakhama A. CD8+ T lymphocytes and leukotriene B4: novel interactions in the persistence and progression of asthma. *J Allergy Clin Immunol*. 2006; 117: 577-582.

Geraghty P, Rogan MP, Greene CM, Boxio RM, Poirier T, O'Mahony M, Belaaouaj A, O'Neill SJ, Taggart CC, McElvaney NG. Neutrophil elastase up-regulates cathepsin B and matrix metalloprotease-2 expression. *J Immunol*. 2007 ;178: 5871-5878.

Gounni AS, Lamkhioued B, Koussih L, Ra C, Renzi PM, Hamid Q. Human neutrophils express the high-affinity receptor for immunoglobulin E (Fc epsilon RI): role in asthma. *FASEB J*. 2001; 15: 940-949.

Gravett CM, Tintinger G, Theron A, Anderson R, Feldman C, Green R. Montelukast sodium: Administration to children to control intermittent asthma. *Clin Med Rev Therap.* 2010; 2: 1-10.

Grynkiewicz G, Poenie M, Tsien RY. A new generation of Ca^{2+} indicators with greatly improved fluorescent properties. *J Biol Chem.* 1985; 260: 3440–3450.

Gueli N, Verrusio W, Linguanti A, De Santis W, Canitano N, Ippoliti F, Marigliano V, Cacciafesta M. Montelukast therapy and psychological distress in chronic obstructive pulmonary disease (COPD): a preliminary report. *Arch Gerontol Geriatr.* 2011; 52: e36-39.

Guichard C, Pedruzzi E, Dewas C, Fay M, Pouzet C, Bens M, Vandewalle A, Ogier-Denis E, Gougerot-Pocidalo MA, Elbim C. Interleukin-8-induced priming of neutrophil oxidative burst requires sequential recruitment of NADPH oxidase components into lipid rafts. *J Biol Chem.* 2007; 280: 37021–37032.

Hallett MB, Lloyds D. Neutrophil priming: the cellular signals that say 'amber' but not 'green'. *Immunol Today.* 1995; 16: 264-268.

Hallmann R, Horn N, Selg M, Wendler O, Pausch F, Sorokin LM. Expression and function of laminins in the embryonic and mature vasculature. *Physiol Rev.* 2005; 85: 979-1000.

Hanania NA. Targeting airway inflammation in asthma: current and future therapies. *Chest.* 2008; 133: 989-998.

Hatzelmann A, Morcillo EJ, Lungarella G, Adnot S, Sanjar S, Beume R, Schudt C, Tenor H. The preclinical pharmacology of roflumilast--a selective, oral phosphodiesterase 4 inhibitor in development for chronic obstructive pulmonary disease. *Pulm Pharmacol Ther.* 2010; 23: 235-256.

- Hay DW, Muccitelli RM, Tucker SS, Vickery-Clark LM, Wilson KA, Gleason JG, Hall RF, Wasserman MA, Torphy TJ. Pharmacologic profile of SK&F 104353: a novel, potent and selective peptidoleukotriene receptor antagonist in guinea pig and human airways. *J Pharmacol Exp Ther.* 1987; 243: 474-4781.
- Heimbürger M, Palmlad J. Effects of leukotriene C4 and D4, histamine and bradykinin on cytosolic calcium concentrations and adhesiveness of endothelial cells and neutrophils. *Clin Exp Immunol.* 1996; 103: 454–460.
- Henderson WR Jr, Chi EY, Bollinger JG, et al. Importance of group X-secreted phospholipase A2 in allergen-induced airway inflammation and remodelling in a mouse asthma model. *J Exp Med.* 2007; 204: 865-877.
- Henderson WR Jr, Chiang GK, Tien YT, Chi EY. Reversal of allergen-induced airway remodeling by CysLT1 receptor blockade. *Am J Respir Crit Care Med.* 2006; 173: 718–728.
- Heutinck KM, ten Berge IJ, Hack CE, Hamann J, Rowshani AT. Serine proteases of the human immune system in health and disease. *Mol Immunol.* 2010; 47: 1943-1955.
- Heyworth PG, Badwey JA. Protein phosphorylation associated with the stimulation of neutrophils. Modulation of superoxide production by protein kinase C and calcium. *J Bioenerg Biomembr.* 1990; 22: 1-26.
- Higgs G. Is PDE4 too difficult a drug target? *Curr Opin Investig Drugs.* 2010; 11: 495-498.
- Hiraguchi Y, Nagao M, Hosoki K, Tokuda R, Fujisawa T. Neutrophil proteases activate eosinophil function in vitro. *Int Arch Allergy Immunol.* 2008; 146: 16–21.

Hogg JC, Doerschuk CM. Leukocyte traffic in the lung. *Ann Rev Physiol.* 1995; 57: 97-114.

Holgate ST, Peters-Golden M, Panettieri RA, Henderson WR Jr. Roles of cysteinyl leukotrienes in airway inflammation, smooth muscle function, and remodeling. *J Allergy Clin Immunol.* 2003; 111: S18-34; discussion S34-36

Holmes, B., Page, A. R., Good, R. A. Studies of the metabolic activity of leukocytes from patients with a genetic abnormality of phagocytic function. *J Clin Invest.* 1967; 46: 1422-1432.

Holmsen H, Storm E, Day HJ. Determination of ATP and ADP in blood platelets: a modification of the firefly luciferase assay for plasma. *Anal Biochem.* 1972; 46: 489–501.

Hui Y, Funk CD. Cysteinyl leukotriene receptors. *Biochem Pharmacol.* 2002; 64: 1549-1557.

Iannone MA, Wolberg G, Zimmerman TP. Chemotactic peptide induces cAMP elevation in human neutrophils by amplification of the adenylate cyclase response to endogenously produced adenosine. *J Biol Chem.* 1989; 264: 20177– 20180.

Ilowite J, Webb R, Friedman B, Kerwin E, Bird SR, Hustad CM, Edelman JM. Addition of montelukast or salmeterol to fluticasone for protection against asthma attacks: a randomized, double-blind, multicenter study. *Ann Allergy Asthma Immunol.* 2004; 92: 641-648.

Illumets H, Ryttilä P, Demedts I, Brusselle GG, Sovijärvi A, Myllärniemi M, Sorsa T, Kinnula VL. Matrix metalloproteinases -8, -9 and -12 in smokers and patients with stage 0 COPD. *Int J Chron Obstruct Pulmon Dis.* 2007; 2: 369-379.

- Ito K, Herbert C, Siegle JS, Vuppusetty C, Hansbro N, Thomas PS, Foster PS, Barnes PJ, Kumar RK. Steroid-resistant neutrophilic inflammation in a mouse model of an acute exacerbation of asthma. *Am J Respir Cell Mol Biol.* 2008; 39: 543-550.
- Jatakanon A, Uasuf C, Maziak W, Lim S, Chung KF, Barnes PJ. Neutrophilic inflammation in severe persistent asthma. *Am J Respir Crit Care Med.* 1999; 160: 1532-1539.
- Jeffery PK, Venge P, Gazycki MJ, Egerod I, Dahl R, Faurschou P. Effects of salmeterol on mucosal inflammation in asthma: a placebo-controlled study. *Eur Respir J.* 2002; 20: 1378-1385.
- Johnson M. Effects of β 2-agonists on resident and infiltrating inflammatory cells. *J Allergy Clin Immunol.* 2002; 110: S282–S290.
- Johnson M. Molecular mechanisms of β 2-adrenergic receptor function, response and regulation. *J Allergy Clin Immunol.* 2006; 117: 18–24.
- Jones TR, Labelle M, Belley M, Champion E, Charette L, Ford-Hutchinson AW, et al. Pharmacology of montelukast sodium (Singulair), a potent and selective leukotriene D₄ receptor antagonist. *Can J Physiol Pharmacol.* 1995; 73: 191–201.
- Jung YW, Zindi C, Lai j, Weaver CT, Chaplin DD. Matrix Metalloproteinases Induced by Gr-1+ Cells are Crucial for recruitment of Th Cells into the Airways. *Eur J Immunol.* 2009; 39: 2281-2292.
- Kanaoka Y, Boyce JA. Cysteinyl leukotrienes and their receptors:cellular distribution and function in immune and inflammatory responses. *J Immunol.* 2004; 173: 1503-1510.
- Karathanassis D, Stahelin RV, Bravo J, Perisic O, Pacold CM, Cho W, Williams RL. Binding of the PX domain of p47^{phox} to phosphatidylinositol 3,4-bisphosphate and

phosphatidic acid is masked by an intramolecular interaction. *EMBO J.* 2002; 21: 5057-5068.

Kasama T, Miwa Y, Isozaki T, Odai T, Adachi M, Kunkel SL. Neutrophil-derived cytokines: potential therapeutic targets in inflammation. *Curr Drug Targets Inflamm Allergy.* 2005; 4 :273-279.

Katsuyama M. NOX/NADPH oxidase, the superoxide-generating enzyme: its transcriptional regulation and physiological roles. *J Pharmacol Sci.* 2010; 114: 134-146.

Keith PK, Koch C, Djandji M, et al. Montelukast as add-on therapy with inhaled corticosteroids and long-acting β 2-agonists in the management of patients diagnosed with asthma and concurrent allergic rhinitis (the RADAR trial). *Can Respir J.* 2009; 16: 17–24.

Kessenbrock K, Dau T, Jenne DE. Tailor-made inflammation: how neutrophil serine proteases modulate the inflammatory response. *Mol Med.* 2011; 89: 23-28.

Kessenbrock K, Fröhlich L, Sixt M, Lämmermann T, Pfister H, Bateman A, Belaaouaj A, Ring J, Ollert M, Fässler R, Jenne DE. Proteinase 3 and neutrophil elastase enhance inflammation in mice by inactivating antiinflammatory progranulin. *J Clin Invest.* 2008; 118: 2438-2447.

Kessenbrock K, Plaks V, Werb Z. Matrix metalloproteinases: regulators of the tumor microenvironment. *Cell.* 2010; 141: 52-67.

Knorr B, Nguyen HH, Kearns GL, Villaran C, Boza ML, Reiss TF, Rogers JD, Zhang J, Larson P, Spielberg S. Montelukast dose selection in children ages 2 to 5 years: comparison of population pharmacokinetics between children and adults. *J Clin Pharmacol.* 2001; 41: 612-619.

Kobayashi SD, Voyich JM, Burlak C, DeLeo FR. Neutrophils in the innate immune response. *Arch Immunol Ther Exp (Warsz)*. 2005; 53: 505-517.

Köhrmann A, Kammerer U, Kapp M, Dietl J, Anacker J. Expression of matrix metalloproteinases (MMPs) in primary human breast cancer and breast cancer cell lines: New findings and review of the literature. *BMC Cancer*. 2009; 9: 188.

Kong MYF, Gaggar A, Li Y, Winkler M, Blalock E, Clancy JP. Matrix Metalloproteinase Activity in Pediatric Acute Lung Injury. *Int J Med Sci*. 2009; 6: 9-17.

Korn D, Van den Brande P, Potvin E, et al. Efficiency of add-on montelukast in patients with non-controlled asthma: a Belgian open-label study. *Curr Med Res Opin*. 2009; 25: 489–497.

Kumar SD, Krishnamurthy K, Manikandan J, Pakeerappa PN, Pushparaj PN. Deciphering the key molecular and cellular events in neutrophil transmigration during acute inflammation. *Bioinformation*. 2011; 6: 111-114.

Lamblin C, Gosset P, Tillie-Leblond I, Saulnier F, Marquette CH, Wallaert B, Tonnel AB. Bronchial neutrophilia in patients with noninfectious status asthmaticus. *Am J Respir Crit Care Med*. 1998; 157: 394-402.

Langlois A, Ferland C, Tremblay GM, Laviolette M. Montelukast regulates eosinophil protease activity through a leukotriene-independent mechanism. *J Allergy Clin Immunol*. 2006; 118: 113-119.

Lapouge K, Smith SJ, Walker PA, Gamblin SJ, Smerdon SJ, Rittinger K. Structure of the TPR domain of p67phox in complex with Rac.GTP. *Mol Cell*. 2000; 6: 899-907.

- Lärfars G, Lantoine F, Devynck MA, Palmlad J, Gyllenhammar H. Activation of nitric oxide release and oxidative metabolism by leukotrienes B4, C4 and D4 in human polymorphonuclear leukocytes. *Blood*. 1999; 93: 1399–1405.
- Laviolette M, Malmstrom K, Lu S, Chervinsky P, Pujet JC, Peszek I, Zhang J, Reiss TF. Montelukast added to inhaled beclamethasone in treatment of asthma. *Am J Respir Crit Care Med*. 1999; 160: 1862–1868.
- Lau WK, Chow AW, Au SC, Ko WH. Differential inhibitory effects of CysLT(1) receptor antagonists on P2Y(6) receptor-mediated signaling and ion transport in human bronchial epithelia. *PLoS One*. 2011; 6: e22363.
- Lazarus SC, Chinchilli VM, Rollings NJ, Boushey HA, Cherniack R, Craig TJ, Deykin A, DiMango E, Fish JE, Ford JG, Israel E, Kiley J, Kraft M, Lemanske RF Jr, Leone FT, Martin RJ, Pesola GR, Peters SP, Sorkness CA, Szeffler SJ, Wechsler ME, Fahy JV; National Heart Lung and Blood Institute's Asthma Clinical Research Network. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma. *Am J Respir Crit Care Med*. 2007; 175: 783-790.
- Lee K-Y, Ho S-C, Lin H-C, Lin SM, Liu CY, Huang CD, Wang CH, Chung KF, Kuo HP. Neutrophil-derived elastase induces TGF- β 1 secretion in human airway smooth muscle. *Am J Respir Cell Mol Biol*. 2006; 35: 407–414.
- Leuenroth SJ, Grutkoski PS, Ayala A, Simms HH. The loss of Mcl-1 expression in human polymorphonuclear leukocytes promotes apoptosis. *J Leukoc Biol*. 2000; 68: 158-166.
- Lew PD, Monod A, Waldvogen FA, Pozzan T. Role of cytosolic free calcium and phospholipase C in leukotriene-B4-stimulated secretion in human neutrophils.

Comparison with the chemotactic peptide formyl-methionyl-leucyl-phenylalanine. *Eur J Biochem.* 1987; 162: 161–168.

Lewis EM, Sergeant S, Ledford B, Stull N, Dinauer MC, McPhail LC. Phosphorylation of p22^{phox} on threonine 147 enhances NADPH oxidase activity by promoting p47^{phox} binding. *J Biol Chem.* 2010; 285: 2959-2967.

Lima JJ. Treatment heterogeneity in asthma: genetics of response to leukotriene modifiers. *Mol Diagn Ther.* 2007; 11 :97-104.

Liu D, Ge S, Zhou G, Xu G, Zhang R, Zhu W, Liu Z, Cheng S, Liu X. Montelukast inhibits matrix metalloproteinases expression in atherosclerotic rabbits. *Cardiovasc Drugs Ther.* 2009; 23: 431-437.

Liu Z, Zhou X, Shapiro SD, Shipley JM, Twining SS, Diaz LA, Senior RM, Werb Z. The serpin alpha1-proteinase inhibitor is a critical substrate for gelatinase B/MMP-9 in vivo. *Cell.* 2000; 102: 647-655.

Lötvall J, Akdis CA, Bacharier LB, Bjermer L, Casale TB, Custovic A, Lemanske RF Jr, Wardlaw AJ, Wenzel SE, Greenberger PA. Asthma endotypes: a new approach to classification of disease entities within the asthma syndrome. *J Allergy Clin Immunol.* 2011; 127: 355-360.

Lovén J, Svitacheva N, Jerre A, et al. Anti-inflammatory activity of β2-agonists in primary lung epithelial cells is independent of glucocorticoid receptor. *Eur Respir J.* 2007; 30: 848–856.

Lundein KA, Sun B, Karlsson L, Fourie AM. Leukotriene B4 receptors BLT1 and BLT2: expression and function in human and murine mast cells. *J Immunol.* 2006; 177: 3439-3447.

MacDowell AL, Peters SP. Neutrophils in asthma. *Curr Allergy Asthma Rep.* 2007; 7: 464–468.

Mackarel AJ, Russell KJ, Ryan CM, Hislip SJ, Rendall JC, FitzGerald MX, O'Connor CM. CD18 dependency of transendothelial neutrophil migration differs during acute pulmonary inflammation. *J Immunol.* 2001; 167: 2839-2846.

Mak JC, Chan-Yeung MM. Reactive oxidant species in asthma. *Curr Opin Pulm Med.* 2006; 12: 7–11.

Mamedova L, Capra V, Accomazzo MR, Gao ZG, Ferrario S, Fumagalli M, Abbracchio MP, Rovati GE, Jacobson KA. CysLT1 leukotriene receptor antagonists inhibit the effects of nucleotides acting at P2Y receptors. *Biochem Pharmacol.* 2005; 71: 115-125.

Maneechoteswan K, Essilfie-Quaye S, Meah S, Kelly C, Kharitonov SA, Adcock IM, Barnes PJ. Formoterol attenuates neutrophilic airway inflammation in asthma. *Chest.* 2005; 128: 1936-1942.

Mansfield PJ, Hinkovska-Galcheva V, Shayman JA, Boxer LA. Granulocyte colony-stimulating factor primes NADPH oxidase in neutrophils through translocation of cytochrome b(558) by gelatinase-granule release. *J Lab Clin Med.* 2002; 140: 9-16.

Martin P. Multi-institutional phase II study of montelukast for the treatment of bronchiolitis obliterans following allogeneic stem cell transplantation in children and adults. <http://www.seattlecca.org/clinical-trials/transplant-NCT00656058.cfm>.

Marwick JA, Adcock IM, Chung KF. Overcoming reduced glucocorticoid sensitivity in airway disease: molecular mechanisms and therapeutic approaches. *Drugs.* 2010; 70: 929-948.

- Mayerle J, Schnekenburger J, Krüger B, Kellermann J, Ruthenbürger M, Weiss FU, Nalli A, Domschke W, Lerch MM. Extracellular cleavage of E-cadherin by leukocyte elastase during acute experimental pancreatitis in rats. *Gastroenterology*. 2005; 129: 1251-1267.
- McCawley LJ, Matrisian LM. Matrix metalloproteinases: They're not just for matrix anymore! *Curr Opin Cell Biol*. 2001; 13: 534-540.
- McFadden ER. Inhaled glucocorticoids and acute asthma: therapeutic breakthrough or non-specific effect? *Am J Respir Crit Care Med*. 1998; 157: 677–678.
- Merck research Laboratory: Data on file.http://www.merck.com/product/usa/pi_circulars/s/singulair/singulair_pi.pdf.
- Minkenberg I, Ferber E . Lucigenin-dependent chemiluminescence as a new assay for NADPH-oxidase activity in particulate fractions of human polymorphonuclear leukocytes. *J Immunol Methods*. 1984; 71: 61–67.
- Monteiro AP, Pinheiro CS, Luna-Gomes T, Alves LR, Maya-Monteiro CM, Porto BN, Barja-Fidalgo C, Benjamim CF, Peters-Golden M, Bandeira-Melo C, Bozza MT, Canetti C. Leukotriene B₄ mediates neutrophil migration induced by heme. *J Immunol*. 2011; 86: 6562-6567.
- Moore AR, Willoughby DA. The role of cAMP regulation in controlling inflammation. *Clin Exp Immunol*. 1995; 101: 387–389.
- Mundell SJ, Olah ME, Panettieri RA, Benovic JL, Penn RB. Regulation of G-protein-coupled receptor-adenyl cyclase responsiveness in human airway smooth muscle by exogenous and autocrine adenosine. *Am J Respir Cell Mol Biol*. 2001; 24: 155–163.

Murphy PM. Neutrophil receptors for interleukin-8 and related CXC chemokines.

Semin Hematol. 1997; 34: 311-318.

Murphy RC, Hammaström S, Samuelsson B. and C Leukotriene, slow –reacting substance from murine mastocytoma cells. **Proc Natl Acad USA.** 1979; 76: 4275-4279.

Muz MH, Deveci F, Bulut Y, Ilhan N, Yekeler H, Turgut T. The effects of low dose leukotriene receptor antagonist therapy on airway remodeling and cysteinyl leukotriene expression in a mouse asthma model. **Exp Mol Med.** 2006; 38: 109–118.

Nadif R, Siroux V, Oryszczyn MP, Ravault C, Pison C, Pin I, Kauffmann F; Epidemiological study on the Genetics and Environment of Asthma (EGEA).

Heterogeneity of asthma according to blood inflammatory patterns. **Thorax.** 2009; 64: 374-380.

Naik S, Billington CK, Pascual RM, Deshpande D, Stefano F, Kohout T, Eckman DM, Benovic JL, Penn RB. Regulation of cysteinyl leukotriene type 1 receptor internalization and signalling. **J Biol Chem.** 2005; 280: 8722–8732.

Narala VR, Adapala RK, Suresh MV, Brock TG, Peters-Golden M, Reddy RC. Leukotriene B4 is a physiologically relevant endogenous peroxisome proliferator-activated receptor-alpha agonist. **J Biol Chem.** 2010; 285: 22067-22074.

National Heart, Lung and Blood Institute, National Institutes of Health, US Department of Health and Human Services. Expert panel report 3: guidelines for the diagnosis and management of asthma. 2007; Section 2, p.1.

Nayak A, Langdon RB. Montelukast in the treatment of allergic rhinitis. An evidence-based review. **Drugs.** 2007; 67: 887–901.

Nick JA, Avdi NJ, Young SK, Knall C, Gerwins P, Johnson GL, Worthen GS.

Common and distinct intracellular signaling pathways in human neutrophils utilized by platelet activating factor and FMLP. *J Clin Invest.* 1997; 99: 975–986.

Obinata H, Yokomizo T, Shimizu T, et al. Glucocorticoids up-regulate leukotriene B4 receptor-1 expression during neutrophilic differentiation of HL-60 cells. *Biochem Biophys Res Comm.* 2003; 309: 114–119.

Ohnishi H, Miyahara N, Dakhama A, Takeda K, Mathis S, Haribabu B, Gelfand EW. Corticosteroids enhance CD8+ T cell-mediated airway hyperresponsiveness and allergic inflammation by upregulating leukotriene B4 receptor 1. *J Allergy Clin Immunol.* 2008; 121: 864-871.e4.

Ohnishi H, Miyahara N, Gelfand EW. The role of leukotriene B₄ in allergic diseases. *Allergol Int.* 2008; 57: 291-298.

Owen CA and Campbell EJ. Neutrophil proteinases and matrix degradation. The cell biology of pericellular proteolysis. *Semin Cell Biology.* 1995; 6: 367–376.

Padrines M, Wolf M, Walza A, Baggiolini M. Interleukin-8 processing by neutrophil elastase, cathepsin G and proteinase-3. *FEBS Letters.* 1994; 352: 231-235

Page CP, Spina D. Phosphodiesterase inhibitors in the treatment of inflammatory diseases. *Handb Exp Pharmacol.* 2011; 204: 391-414.

Palmlad J, Gyllenhammar H, Lindgren JA, Malmsten CL. Effects of leukotrienes and f-Met-Leu-Phe on oxidative metabolism of neutrophils and eosinophils. *J Immunol.* 1984; 132: 3041-3045.

Peters-Golden M and WR Henderson, Mechanisms of disease: Leukotrienes. *New Engl J Med.* 2007; 357: 1841-1854.

Peters-Golden M, Brock TG. 5-lipoxygenase and FLAP. *Prostaglandins Leukot Esent Fatty Acids*. 2003; 69: 99-109.

Pétrin D, Turcotte S, Gilbert AK, Rola-Pleszczynski M, Stankova J. The anti-apoptotic effect of leukotriene B4 in neutrophils: a role for phosphatidylinositol 3-kinase, extracellular signal-regulated kinase and Mcl-1. *Cell Signal*. 2006; 18: 479-487.

Pettit EJ, Hallett MB. Two distinct Ca²⁺ storage and release sites in human neutrophils. *Leukoc Biol*. 1998; 63: 225-232.

Pham CTN. Neutrophil serine proteases fine-tune the inflammatory response. *Int J Biochem Cell Biol*. 2008; 40: 1317–1333.

Ponce L, Arjona M, Blanco G, Alvarez S, Arcila E, Ortega A, Nuñez D, Verzura J, Tovar R, Bethencourt S, Riera R, Mora-Orta S, Corado J. The effect of montelukast in a model of gouty arthritis induced by sodium monourate crystals. The effect of montelukast in a model of gouty arthritis induced by sodium monourate crystals. *Invest Clin*. 2011; 52: 15-22.

Prikk K, Maisi P, Pirilä E, Reintam MA, Salo T, Sorsa T, Sepper R. Airway obstruction correlates with collagenase-2 (MMP-8) expression and activation in bronchial asthma. *Lab Invest*. 2002; 82: 1535-1545.

Rabe KF. Update on roflumilast, a phosphodiesterase 4 inhibitor for the treatment of chronic obstructive pulmonary disease. *Br J Pharmacol*. 2011; 163: 53-67.

Rabinovitch N, Strand M, Stuhlman K, Gelfand EW. Exposure to tobacco smoke increases leukotriene E4-related albuterol usage and response to montelukast. *J Allergy Clin Immunol*. 2008; 121: 1365-1371.

Ramires R, Caiaffa MF, Tursi A, Haeggström JZ, Macchia L. Novel inhibitory effect on 5-lipoxygenase activity by the anti-asthma drug montelukast. *Biochem Biophys Res Commun.* 2004; 324: 815-821.

Raptis SZ, Shapiro SD, Simmons PM, Cheng AM, Pham CT. Serine protease cathepsin G regulates adhesion-dependent neutrophil effector functions by modulating integrin clustering. *Immunity.* 2005; 22: 679-691.

Reilly DM, Parslew R, Sharpe GR, Powell S, Green MR. Inflammatory mediators in normal, sensitive and diseased skin types. *Acta Derm Venereol.* 2000; 80: 171-174.

Riccioni G, Bucciarelli T, Mancini B, Di Ilio C, D'Orazio N. Antileukotriene drugs: clinical application, effectiveness and safety. *Curr Med Chem.* 2007; 14: 1966-1977.

Robinson AJ, Kashanin D, O'Dowd F, Williams V, Walsh GM. Montelukast inhibition of resting and GM-CSF-stimulated eosinophil adhesion to VCAM-1 under flow conditions appears independent of cysLT(1)R antagonism. *J Leukoc Biol.* 2008; 83: 1522-1529.

Robledo, A. Papaioannou, B. Ochietti, C. Beauchemin, D. Legault and A. Cantin et al., ICAM-1 isoforms: Specific activity and sensitivity to cleavage by leukocyte elastase and cathepsin G. *Eur J Immun.* 2003; 33: 1351–1360.

Rubin P, Mollison KW. Pharmacotherapy of diseases mediated by 5-lipoxygenase pathway eicosanoids. *Prostaglandins Other Lipid Mediat.* 2007; 83: 188-197.

Rubinstein I, Kumar B, Schriever C. Long-term montelukast therapy in moderate to severe COPD- a preliminary observation. *Respir Med.* 2004; 98: 134–138.

Ruiz-Velasco V, Zhong J, Hume JR, Keef KD. Modulation of Ca^{2+} channels by cyclic nucleotide cross activation of opposing protein kinases in rabbit portal vein. *Circ Res.* 1998; 82: 557–565.

- Salmon MD, Ahluwalia J. Discrimination between receptor- and store-operated Ca^{2+} influx in human neutrophils. *Cell Immunol.* 2010; 265: 1-5.
- Salpeter SR, Buckley NS, Ormiston TM, Salpeter EE. Meta-analysis: effect of long-acting beta-agonists on severe asthma exacerbations and asthma-related deaths. *Ann Intern Med.* 2006; 144: 904-912.
- Sampson AP, Castling DP, Green CP, Price JF. Persistent increase in plasma and urinary leukotrienes after acute asthma. *Arch Dis Child.* 1995; 73: 221-225.
- Samuelsson B. Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation. *Science.* 1983; 220: 568-575.
- Sanz MJ, Cortijo J, Morcillo EJ. PDE4 inhibitors as new anti-inflammatory drugs: effects on cell trafficking and cell adhesion molecules expression. *Pharmacol Ther.* 2005; 106: 269-297.
- Scapini P, Lapinet-Vera JA, Gasperini S, Calzetti F, Bazzoni F, Cassatella MA. The neutrophil as a cellular source of chemokines. *Immunol Rev.* 2000; 177: 195-203.
- Schaff UY, Dixit N, Procyk E, Yamayoshi I, Tse T, Somin SI. Orai1 regulates intracellular calcium, arrest, and shape polarization during neutrophil recruitment in shear flow. *Blood.* 2010; 115: 657-666.
- Sears MR. The addition of long-acting beta-agonists to inhaled corticosteroids in asthma. *Curr Opin Pulm Med.* 201; 17: 23-28.
- Sener G, Sehirli O, Cetinel S, Ercan F, Yüksel M, Gedik N, Yeğen BC. Amelioration of sepsis-induced hepatic and ileal injury in rats by the leukotriene receptor blocker montelukast. *Prostaglandins Leukot Essent Fatty Acids.* 2005; 73: 453-462.

Serezani CH, Ballinger MN, Aronoff DM, Peters-Golden M. Cyclic AMP: master regulator of innate immune cell function. *Am J Respir Cell Mol Biol.* 2008; 39: 127-132.

Shapiro SD. Neutrophil elastase: path clearer, pathogen killer, or just pathologic? *Am J Respir Cell Mol Biol.* 2002; 26: 266-268.

Sheppard FS, Kelher MR, Moore EE, McLaughlin NJD, Banerjee A, Silliman CC. Structural organization of the neutrophil NADPH oxidase: phosphorylation and translocation during priming and activation. *J Leukoc Biol.* 2005; 78: 1025-1042.

Silliman CC, Elzi DJ, Ambruso DR, Musters RJ, Hamiel C, Harbeck RJ, Paterson AJ, Bjornsen AJ, Wyman TH, Kelher M, England KM, McLaughlin-Malaxecheberria N, Barnett CC, Aiboshi J, Bannerjee A. Lysophosphatidylcholines prime the NADPH oxidase and stimulate multiple neutrophil functions through changes in cytosolic calcium. *J Leukoc Biol.* 2003; 73: 511-524.

Singh RK, Gupta S, Dastidar S, Ray A. Cysteinyl leukotrienes and their receptors: molecular and functional characteristics. *Pharmacol.* 2010; 85: 336-349.

Sousa AR, Parikh A, Scadding G, Corrigan CJ, Lee TH. Leukotriene-receptor expression on nasal mucosal inflammatory cells in aspirin-sensitive rhinosinusitis. *N Engl J Med.* 2002; 347: 1493-1499.

Steel HC, Anderson R. Dissociation of the PAF-receptor from NADPH oxidase and adenylate cyclase in human neutrophils results in accelerated influx and delayed clearance of cytosolic calcium. *Br J Pharmacol.* 2002; 136: 81-89.

Steel HC, Tintinger GR, Theron AJ, Anderson R. Itraconazole-mediated inhibition of calcium entry into platelet-activating factor-stimulated human neutrophils is due to

interference with production of leukotriene B4. *Clin Exp Immunol.* 2007; 150: 144–150.

Stelmach I, Korzeniewska A, Stelmach W, Majak P, Grzelewski T, Jerzynska J. Effects of montelukast treatment on clinical and inflammatory variables in patients with cystic fibrosis. *Ann Allergy Asthma Immunol.* 2005; 95: 372-380.

Strickland I, Kisich K, Hauk PJ, Vottero A, Chrousos GP, Klemm DJ, Leung DY. High constitutive glucocorticoid receptor beta in human neutrophils enables them to reduce their spontaneous rate of cell death in response to corticosteroids. *J Exp Med.* 2001; 193: 585-593.

Su WH, Chen HI, Jen CJ. Differential movements of VE-cadherin and PECAM-1 during transmigration of polymorphonuclear leukocytes through human umbilical vein endothelium. *Blood.* 2002; 100: 3597-3603.

Sugiura H, Ichinose M. Oxidative and nitrative stress in bronchial asthma. *Antioxid Redox Signal.* 2008; 10: 785–797.

Suzuki T, Wang W, Lin JT, Shirato K, Mitsuhashi H, Inoue H. Aerosolized neutrophil elastase induces airway constriction and hyperresponsiveness with protection by intravenous pretreatment with half-length secretory leukoprotease inhibitor. *Am J Respir Crit Care Med.* 1996; 153: 1405–1411.

Tager AM, Luster AD. BLT1 and BLT2: the leukotriene B(4) receptors.

Prostaglandins Leukot Essent Fatty Acids. 2003; 69: 123-34.

Tandon A, Sinha S. Structural insights into the binding of MMP-9 inhibitors. *Bioinformation.* 2011; 5: 310-314.

Thelen M, Didichenko SA. G-protein coupled receptor-mediated activation of PI 3-kinase in neutrophils. *Ann N Y Acad Sci.* 1997; 832: 368-382.

- Theron AJ, Gravett CM, Steel HC, Tintinger GR, Feldman C, Anderson R. Leukotrienes C₄ and D₄ sensitize human neutrophils for hyperreactivity to chemoattractants. *Inflamm Res.* 2009; 58: 263–268.
- Theron AJ, Steel HC, Tintinger GR, Anderson R. Endogenous adenosine regulates neutrophil pro-inflammatory activities by cyclic AMP-dependent accelerated clearance of cytosolic calcium. *Inflamm Res.* 2002; 51: 594-602.
- Tintinger G, Steel HC, Anderson R. Taming the neutrophil: calcium clearance and influx mechanisms as novel targets for pharmacological control. *Clin Exp Immunol.* 2005; 141: 191-200.
- Tintinger G, Steel HC, Theron AJ, Anderson R. Pharmacological control of neutrophil-mediated inflammation: Strategies targeting calcium handling by activated polymorphonuclear leucocytes. *Drug Design Develop Therapy.* 2008; 2: 95-104.
- Tintinger GR, Anderson R, Theron AJ, Ramafi G, Ker JA. Comparison of the effects of selective and non-selective β-adrenergic agonists on the pro-inflammatory activities of human neutrophils in vitro. *Inflammation.* 2000; 24: 239–249.
- Tintinger GR, Theron AJ, Steel HC, Anderson R. Accelerated calcium influx and hyperactivation of neutrophils in chronic granulomatous disease. *Clin Exp Immunol.* 2001; 123: 254–263.
- Tokuriki S, Ohshima Y, Yamada A, Ohta N, Tsukahara H, Mayumi M. Leukotriene D4 enhances the function of endothelin-1-primed fibroblasts. *Clin Immunol.* 2007; 125: 88-94.
- Torphy TJ. Phosphodiesterase isozymes: molecular targets for novel antiasthma agents. *Am J Respir Crit Care Med.* 1998; 157: 351-370.

Turtay MG, Firat C, Samdanci E, Oguzturk H, Erbatur S, Colak C. Effects of montelukast on burn wound healing in a rat model. *Clin Invest Med.* 2010; 33: E413-421.

Underwood DC, Kotzer CJ, Bochnowicz S, Osborn RR, Luttmann MA, Hay DW, Torphy TJ. Comparison of phosphodiesterase III, IV and dual III/IV inhibitors on bronchospasm and pulmonary eosinophils influx in guinea pigs. *J Pharmacol Exp Ther.* 1994; 270: 250–259.

Uozumi N, Kune K, Nagase T, et al. Role of cytosolic phospholipase A2 in allergic response and parturition. *Nature.* 1997; 390: 618-622.

Upham JW, James AL. Remission of asthma: The next therapeutic frontier? *Pharmacol Ther.* 2011; 130: 38-45.

Urban CF, Ermert D, Schmid M, Abu-Abed U, Goosmann C, Nacken W, Brinkmann V, Jungblut PR, Zychlinsky A. Neutrophil extracellular traps contain calprotectin, a cytosolic protein complex involved in host defense against *Candida albicans*. *PLoS Pathog.* 2009; 5(10): e1000639.

Van Rensen EL, Sont JK, Evertse CE, Willems LN, Mauad T, Hiemstra PS, Sterk PJ; AMPUL Study Group. Bronchial CD8 cell infiltrate and lung function decline in asthma. *Am J Respir Crit Care Med.* 2005; 172: 837-841.

Van Weel C, Bateman ED, Bousquet J, et al. Asthma management pocket reference 2008. *Allergy.* 2008; 63: 997–1004.

Verleden GM, Verleden SE, Vos R, De Vleeschauwer SI, Dupont LJ, Van Raemdonck DE, Vanaudenaerde BM. Montelukast for bronchiolitis obliterans syndrome after lung transplantation: a pilot study. *Transpl Int.* 2011; 24: 651-656.

Vignola AM, Kips J, Bousquet J. Tissue remodeling as a feature of persistent asthma. *J Allergy Clin Immunol.* 2000; 105: 1041-1053.

Voisin MB, Woodfin A, Nourshargh S. Monocytes and neutrophils exhibit both distinct and common mechanisms in penetrating the vascular basement membrane in vivo. *Arterioscler Thromb Vasc Biol.* 2009; 29: 1193-1199.

Walsh GM. Novel cytokine-directed therapies for asthma. *Discov Med.* 2011; 11: 283-291.

Wang L, Du C, Lv J, Wei W, Cui Y, Xie X. Antiasthmatic Drugs Targeting the Cysteinyl Leukotriene Receptor 1 Alleviate Central Nervous System Inflammatory Cell Infiltration and Pathogenesis of Experimental Autoimmune Encephalomyelitis. *J Immunol.* 2011; 187: 2336-2345.

Wang P, Wu P, Ohleth KM, Egan RW, Billah MM. Phosphodiesterase 4B2 is the predominant phosphodiesterase species and undergoes differential regulation of gene expression in human monocytes and neutrophils. *Mol Pharmacol.* 1999; 56: 170–174.

Wang S, Voisin MB, Larbi KY, Dangerfield J, Scheiermann C, Tran M, Maxwell PH, Sorokin L, Nourshargh S. Venular basement membranes contain specific matrix protein low expression regions that act as exit points for emigrating neutrophils. *J Exp Med.* 2006; 203: 1519-1532.

Wang, J.P. Dangerfield, R.E. Young, S. Nourshargh. PECAM-1, alpha6 integrins and neutrophil elastase cooperate in mediating neutrophil transmigration, *J Cell Sci.* 2005; 118: 2067–2076.

Ward C, Chilvers ER, Lawson MF, Pryde JG, Fujihara S, Farrow SN, Haslett C, Rossi AG. NF-kappaB activation is a critical regulator of human granulocyte apoptosis in vitro. *J Biol Chem.* 1999; 274: 4309-4318.

Wenzel SE, Szeffler SJ, Leung DY, Sloan SI, Rex MD, Martin RJ. Bronchoscopic evaluation of severe asthma. Persistent inflammation associated with high dose glucocorticoids. *Am J Respir Crit Care Med.* 1997; 156: 737-743.

Wenzel SE, Trudeau JB, Westcott JY, Beam WR, Martin RJ. Single oral dose of prednisone decreases leukotriene B4 production by alveolar macrophages from patients with nocturnal asthma but not control subjects: relationship to changes in cellular influx and FEV1. *J Allergy Clin Immunol.* 1994; 94: 870-881.

Wenzel SE. Asthma: defining of the persistent adult phenotypes. *Lancet.* 2006; 368: 804-813.

Wright HL, Moots RJ, Bucknall RC, Edwards SW. Review. Neutrophil function in inflammation and inflammatory diseases. *Rheumatol (Oxford).* 2010; 49: 1618-1631.

Wu Y, Zhou C, Tao J, Li S. Montelukast prevents the decrease of interleukin-10 and inhibits NF-kappa B activation in inflammatory airway of asthmatic guinea pigs. *Can J Physiol Pharmacol.* 2006; 84: 531–537.

Xu et al., 2005 M. Xu, E. Bruno, J. Chao, S. Huang, G. Finazzi and S.M. Fruchtman et al., Constitutive mobilization of CD34+ cells into the peripheral blood in idiopathic myelofibrosis may be due to the action of a number of proteases. *Blood.* 2005; 105: 4508–4515.

Xu Y, Zhao Y, Huang H, Chen G, Wu X, Wang Y, Chang W, Zhu Z, Feng Y, Wu D. Expression and function of toll-like receptors in multiple myeloma patients: toll-like

receptor ligands promote multiple myeloma cell growth and survival via activation of nuclear factor-kappaB. *Br J Haematol.* 2010; 150: 543-553.

Yang L, Froio RM, Sciuto TE, Dvorak AM, Alon R, Luscinskas FW. ICAM-1 regulates neutrophil adhesion and transcellular migration of TNF-alpha-activated vascular endothelium under flow. *Blood.* 2005; 106: 584-592.

Yang Y, Luo J, Kazumura K, Takeuchi K, Inui N, Hayashi H, Ohashi K, Watanabe H. Cilostazol suppresses adhesion of human neutrophils to HUVECs stimulated by FMLP and its mechanisms. *Life Sci.* 2006; 79: 629–636.

Yokomizo T, Kato K, Hagiya H, Izumi T, Shimizu T. Hydroxyeicosanoids bind to and activate the low affinity leukotriene B4 receptor, BLT2. *J Biol Chem.* 2001; 276: 12454-12459.

Yoshisue H, Kirkham-BrownJ, Healy E, Holgate ST, Sampson AP, Davies DE. Cysteinyl leukotrienes synergize with growth factors to induce proliferation of human bronchial fibroblasts. *J Allergy Clin Immunol.* 2007; 119: 132-140.

Zhu J, Qiu YS, Figueroa DJ, Bandi V, Galczenksi H, Hamada K, Guntupalli KK, Evans JF, Jeffery PK. Localization and upregulation of cysteinyl leukotriene-1 receptor in asthmatic bronchial mucosa. *Am J Respir Cell Mol Biol.* 2005; 33: 531–540.