Patent Annotations:

The patents annotated in this section have been selected by the authors of this issue as the most important patents of relevance to their field.

VEGF, ANGIOPOIETIN-1 AND -2 IN BRONCHIAL ASTHMA: NEW MOLECULAR TARGETS IN AIRWAY ANGIOGENESIS AND MICROVASCULAR REMODELING

1. **Inhibitors of vascular endothelial growth factor activity, their uses and processes for their production.** ***Davis-Smyth, T.L., Chen, H.H., Presta, L., Ferrara, N.: US20056897294B2 (2005).***

Commentary:

Novel chimeric VEGF receptor proteins comprise of amino acid sequences derived from the vascular endothelial growth factor (VEGF) receptors FLT-1, KDR and the murine homolog of the human KDR receptor, FLK-1, which are capable of binding to VEGF and inhibit endothelial cell pro-liferation and angiogenesis.

2. **Anti-VEGF antibodies,** ***Baca, M., Wells, J.A., Presta, L.G., Lowman, H.B., Chen, Y.M.-Y.: US20067060269B1 (2006).***

Commentary:

The present invention discloses humanized and variant anti-VEGF antibodies and their uses. The anti-VEGF antibodies have strong binding activities for VEGF which inhibit VEGF-induced proliferation of endothelial cells and also tumor growth.

3. **Therapeutic agents and methods of use thereof for the modulation of angiogenesis,** ***Olson, G.L., Self, C., Lee, L., Cook, C.M., Birktoft, J.: US20067037890B2 (2006).***

Commentary:

The invention provides angiogenesis inhibitor compounds which comprise of a Fumagillin core that inhibits methionine aminopeptidase 2 (MetAP-2) coupled to a peptide. The invention also describes the method of treating an angiogenic disease like cancer.

4. **Methods of treatment of inflammatory diseases using specific binding agents of human angiopoietin-2,** ***Oliner, J.D., Min, H.: EP1615952A2 (2006).***

Commentary:

Peptides that bind to Ang-2 and peptibodies comprising of the peptides are disclosed. The invention also describes the methods of making such peptides and peptibodies, and methods of treatment by using these peptides and peptibodies.

CD48 AS A NOVEL TARGET IN ASTHMA THERAPY

1. **Human cDNAs and proteins and uses thereof,** ***Bejanin, S., Tanaka, H.: US20067005500 (2006).***

Commentary:

The invention discusses GENSET polynucleotides and polypeptides which are used as reagents in forensic analyses, as chromosome markers, as tissue/cell/organelle-specific markers, in the production of expression vectors. They are also used for screening and diagnosing assays of abnormal GENSET expression and/or biological activity and for screening compounds that may be used in the treatment of GENSET-related disorders.

NOVEL STRATEGIES FOR THE TREATMENT OF ASTHMA

1. **Pyrazoloisoquinoline derivatives for inhibiting NF dollar G (K) B-inducing kinase (NIK),** ***Flohr, S., Naumann, T.: WO04005287A1(2004).***

Commentary:

The invention relates to compounds useful in the preparation of medicaments for prophylaxis and the treatment of diseases which are conducive to the progression of NIK activity.

2. **Novel indazole carboxamides and their use,** ***Kerns, J.K., Edwards, C.: WO06002434A2 and WO06002434A3 (2006).***

Commentary:

Novel indazole carboxamide derivatives are discussed in this invention. These derivatives are useful in the treatment of disorders associated with inappropriate IKK2 (also known as IKKss) activity, such as rheumatoid arthritis, asthma, and COPD (chronic obstructive pulmonary disease).

3. **Combinations of statins with bronchodilators,** ***Lindmark, B., Thoren, A.: WO06008437A1 (2006).***

Commentary:

The invention provides combinations comprising of bronchodilators, glucocorticosteroids and HMG-CoA reductase inhibitors, which are used in the treatment of respiratory disorders such as chronic obstructive pulmonary disease (COPD).

4. **Conjugates with anti-inflammatory activity,** ***Mercep, M., Mesic, M., Tomaskovic, L., Markovic, S., Poljak, V., Sijan, G., Selmani, S.: WO06046123A2 (2006).***

Commentary:

The present invention discusses new compounds, which are used in the treatment of inflammatory diseases and conditions in humans and animals.

5. **Decladinosyl-macrolides with anti-inflammatory activity,** ***Culic, O., Bosnar, M., Alihodzic, S., Lazarevski, G., Istuk Marusic, Z., Hutinec, A., Vela, V., Kragol, G.: WO06077501A2 (2006).***

Commentary:

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The present invention discusses novel semi-synthetic macrolides, which are used in the treatment of inflammatory diseases and especially those diseases associated with excessive secretion of TNF-α, IL-1, IL-6, IL-8, IL-2 or IL-5; and/or inhibitor of excessive lymphocyte proliferation; and/or excessive granulocyte degranulation.

6. **Metalloproteinase inhibitors,** ***Eriksson, A., Lepistö, M., Lundkvist, M., Munck AR., Stenvall, K., Zlatoidsky, P.: US20067132434 (2006).***

Commentary:

The present invention discusses compounds which are helpful as metalloproteinase inhibitors, especially as inhibitors of MMP12, also known as macrophage elastase or metalloelastase.

ANTI-TUMOR NECROSIS FACTOR-ALPHA (TNF-α) TREATMENT STRATEGIES IN CROHN'S DISEASE

1. **Antibodies to cytokines in the prevention and treatment of inflammatory bowel disease,** ***King, J.A., Worledge, K.L., Stafford, D.C.: US2005053604A1 (2005), US20036663864 (2003) and US20026395273 (2002).***

Commentary:

The present invention describes methods which are used for treating inflammatory bowel disease such as Crohn's disease in animals as well as in humans.

2. **Suppression of TNF-g(α) and IL-12 in therapy,** ***Feldmann, M., Malfait, A.-M.A.M., Butler, D.M., Brennan, F.M., Maini, R.N.: EP0936923B1 (2003), EP0936923B1 (1999) and WO09822137A1 (1998).***

Commentary:

The invention discloses methods for treating and/or preventing TNF alpha-mediated diseases, which include rheumatoid arthritis, Crohn's disease and acute as well as chronic immune diseases associated with transplantation. These compositions comprise of a TNF antagonist and an IL-12 antagonist.

3. **Use of tumor necrosis factor alpha (TNF-alpha) and vascular endothelial growth factor (VEGF) for the manufacture of a therapeutic composition,** ***Feldmann, M., Maini, R.N., Paleolog, E.M.: EP1170017A1 (2002).***

Commentary:

The invention discloses methods for treating and/or preventing TNF alpha-mediated diseases, which include rheumatoid arthritis, Crohn's disease and acute as well as chronic immune diseases associated with transplantation. These compositions comprise of a TNF and a VEGF antagonist.

4. **Treatment of inflammatory bowel disease (IBD) with anti-angiogenic compounds,** ***Mazar, A., Danese, S., Fiocchi, C.: WO06124611A1 (2006).***

Commentary:

The present invention discloses inhibitors of angiogenesis, which are therapeutically used for treating inflammatory bowel disease especially Crohn's Disease.

5. **Compositions and methods for the treatment of inflammatory bowel disease utilizing NF-kappaB decoy polynucleotides,** ***Strober, W., Fuss, I., Kitani, A., Fichtner-Feigl, F.: US20060258604A1 (2006).***

Commentary:

The present invention provides a method comprising of NF-kappaB decoy polynucleotide, which is used for treating or preventing inflammatory bowel disease (IBD).

ALLERGIC INFLAMMATION AND THE ORAL MUCOSA

1. **Methods for use of apoptotic cells to deliver antigen to dendritic cells for induction or tolerization of T cells,** ***Albert, M.L., Bhardwaj, N., Steinman, R.M., Inaba, K., Darnell, R.: US20067129037 (2006).***

Commentary:

The invention discloses methods and compositions applied for delivering antigens to dendritic cells, which are capable of inducing antigen-specific cytotoxic T lymphocytes and T helper cells activity used in vaccine therapies.

2. **Oral care formulation,** ***Takeda, H., Noda, Y., Ueki, T., Howashi, K., Tsukamoto, S.: JP2006083100A2 (2006).***

Commentary:

The invention highlights oral care formulation comprising of poly-[gamma]-glutamic acid or poly-[gamma]-glutamic acid and polyphenol, which is used in the treatment of oral disorder.

INFECTIOUS COMPLICATIONS WITH ANTI-TNF α THERAPY IN RHEUMATIC DISEASES: A REVIEW

1. **2, 4-Disubstituted thiazolyl derivatives,** ***Love, C., Van Wauwe, J.P.F., De Brabander, M., Cooymans, L., Vandermaesen, N., Kennis, L.E.J.: US20067105550 (2006).***

Commentary:

The present invention describes 2, 4-disubstituted thiazolyl derivatives having pro-inflammatory cytokine production inhibiting properties and adenosine A.sub.3 receptor blocking properties. The invention also discusses the methods of their preparation and pharmaceutical compositions used for the prevention or the treatment of warm-blooded animals suffering from diseases associated with cytokines or activation of the adenosine A.sub.3 receptor.

2. **2, 4, 5-Trisubstituted thiazolyl derivatives and their anti-inflammatory activity,** ***Love, C.J., De Brabander, M.J., Goncharenko, M., Vandermaesen, N., Sibley, A.W., Noula, C.: US20067138403 (2006).***

Commentary:

The present invention describes 2, 4, 5-trisubstituted thiazolyl derivatives having pro-inflammatory cytokine production inhibiting properties. The invention also discusses the methods of their preparation and pharmaceutical compositions used for the prevention or the treatment of diseases mediated through TNF α and /or IL-12.

3. **Anti-TNF alpha antibodies which selectively inhibit TNF alpha signalling through the p55R,** ***Brown, D.T., Kirby, H., Finney, H.M., Lawson, A.D.G.: WO06056779A2 (2006).***

Commentary:

The present invention relates to anti-TNF alpha antibodies which inhibit TNF alpha signaling through the p55R, which is used for treating autoimmune diseases e.g. rheumatoid arthritis.

4. **Use of TNF alpha antibodies and another drug,** ***Elliot, C.: MX4010498A (2004).***

Commentary:

The invention highlights the use of TNF alpha antibodies and one or more drugs employed for treating autoimmune diseases e.g. rheumatoid arthritis, sepsis, allergy, or multiple sclerosis.

A REVIEW OF RECENT PATENTS CONCERNING THERAPY OF RESPIRATORY DISEASES USING GENE SILENCING BY RNAI (RISC) AND EGS (RNASE P)

1. **RNAi-based therapeutics for allergic rhinitis and asthma,** ***Chen J., Eisen H.N., Ge, Q.: US2006058255A1 (2006).***

Commentary:

The present invention provides novel therapeutic agents for the treatment of a variety of diseases and conditions associated with IgE-mediated hypersensitivity e.g., allergic rhinitis and asthma.

2. **Inhibitors of ribonucleotide reductase subunit 2 and uses thereof,** ***Davis M.E., Heidel J.D., Rossi J.J.: US2006263435A1 (2006).***

Commentary:

The present invention discusses inhibitors of ribonucleotide reductase subunit 2 (R2), and also methods and compositions related to the R2 inhibitors, which include nucleic acids, such as siRNAs.

3. **Nuclease resistant external guide sequences for treating inflammatory and viral related respiratory diseases,** ***Dreyfus D.H.: US2005277613A1 (2005).***

Commentary:

The present invention describes External Guide Sequence (EGS) that targets proteins required for generation and modification of the immunoglobulin and T-cell repertoire, which are useful for the treatment or prevention of inflammatory or related diseases.

4. **Enzymatic nucleic acid-mediated treatment of ocular diseases or conditions related to levels of vascular endothelial growth factor receptor (VEGF-R),** ***Pavco P., McSwiggen J.A., Tinchcomb D., Scobedo J.: US20067034009 (2006).***

Commentary:

The invention provides novel nucleic acid-based compounds and methods for their use to down regulate or inhibit the expression of receptors of VEGF (VEGF-R).

5. **Conjugates and compositions for cellular delivery,** ***Matulic-Adamic J., Beigelman L.: US20067109165 (2006).***

Commentary:

The present invention relates to conjugates, compositions, methods of synthesis, and applications of various therapeutic compounds such as antiviral and chemo-therapeutic agents, which are useful for cellular delivery.

6. **RNAi modulation of RSV and therapeutic uses thereof,** ***Meyers R.: US20060258608A1 (2006).***

Commentary:

The present invention demonstrates respiratory syncytial virus (RSV), which can be inhibited through intranasal administration of iRNA agents, or by parenteral administration of such agents, and the identification of potent iRNA agents from the P, N and L gene of RSV. These agents can reduce RNA levels with both the A and B subtype of RSV.

7. **siRNA treatment of diseases or conditions related to levels of IKK-gamma** ***McSwiggen J.A.: US20067022828 (2006).***

Commentary:

The present invention discusses nucleic acid molecules which include antisense and enzymatic nucleic acid molecules, such as hammerhead ribozymes, DNAzymes, allozymes, aptamers, decoys and siRNA (RNAi), which modulate the expression or function of IKK genes, such as IKK-gamma, IKK-alpha or IKK-beta, and PKR genes.

TARGETING THE TOLL-SYSTEM IN CARDIOVASCULAR SCIENCES

1. **Variant TLR4 nucleic acid and uses thereof,** ***Lorenz, E., Schwartz, D.A., Schutte, B.C.: WO0077204 (2000).***

Commentary:

Identification of polymorphisms at the human TLR4 locus and methods to identify individuals at risk of indications that increase their morbidity and mortality has been discussed in this invention.

2. **Treating vascular disease by inhibiting toll-like receptor-4,** ***Arditi, M., Rajavashisth, T., Shah, P.K.: WO03035110 (2003).***

Commentary:

The invention describes the treatment of atherosclerosis and other vascular diseases such as thrombosis, restenosis after angioplasty and/or stenting and vein-graft disease after bypass surgery, by inhibition of the expression or biologic activity of Toll-like receptor-4 (TLR-4).

3. **Treating vascular disease by inhibiting myeloid differentiation factor 88,** ***Arditi, M., Raja, T.B., Shah, P. K.: WO03051396 (2003).***

Commentary:

The invention describes the treatment of atherosclerosis and other vascular diseases such as thrombosis, restenosis after angioplasty and/or stenting, and vein-graft disease after

bypass surgery, by inhibition of the expression or biologic activity of myeloid differentiation factor 88 (MyD88).

4. **Non-human animal models for diabetic complications and their uses, *Tirabassi, R.S., Kislauskis, E.H., Flanagan, J.F., Guberski, D.L.: WO06021006 (2006).***

Commentary:

The present invention provides methods for generating non-human animal models for diabetic complications by administering a Toll-Like Receptor (TLR) agonist to non-human animal. The invention also provides methods for screening of therapeutic agents which are useful for treating or preventing a diabetic complications or complications including neuropathy, nephropathy, retinopathy, peripheral circulation disorders, erectile dysfunction in male diabetic patients and skin ulcerations.

FEBUXOSTAT: A NOVEL NON-PURINE SELECTIVE INHIBITOR OF XANTHINE OXIDASE FOR THE TREATMENT OF HYPERURICEMIA IN GOUT

1. **Substituted thiazoles, *Robbins, T.A., Zhu, H., Shao, J.: WO05012273A2 (2005) and WO05012273A3 (2005).***
2. **Process for the preparation of substituted thiazoles, *Shao, J., Zhu, H., Robbins, T.A.: CA2533658AA (2005).***
3. **Process for the preparation of substituted thiazoles, *Jun, S.: MX6001201A (2006).***

Commentary:

The invention describes processes for making substituted thiazoles, such as ethyl 2-(4-hydroxyphenyl)-4-methyl-1, 3-thiazole-5-carboxylate, also known as TEI-6720, which is useful for the treatment of gout and hyperuricemia. The compound belongs to a class of substituted thiazoles that inhibit xanthine oxidase and thus block uric acid production.

RECENT PATENTS IN PEMPHIGUS RESEARCH, PROPHYLAXIS, DIAGNOSIS AND TREATMENT IN USA (1988-2006)

1. **Autoimmune disease model animal, *Amagai, M., Nishikawa, T., Suzuki, H., Koyasu, S.: US20067060868 (2006).***

Commentary:

The present invention describes *Pemphigus vulgaris* (PV), being an autoimmune disease involving skin and mucous membrane characterized by blisters formation. The invention also defines non-human mammals showing phenotypes of the autoimmune disease in which the activation of T cells and B cells reactive to the antigen protein for the autoimmune disease, followed by the stable induction of autoantibody which also provides a method for producing them.

2. **Nicotinamide derivatives useful as PDE4 inhibitors, *Bailey, S., Gautier, E.C.L., Magee, T.V., Marfat, A., Mathias, J.P., McLeod, D.G., Monaghan, S.M., Stammen, B.L.C.: US20056949573 (2005).***

Commentary:

The invention provides nicotinamide derivatives and processes involved in their preparation, the intermediates used, compositions containing them and their uses. These derivatives are useful in the treatment of numerous diseases e.g. inflammatory, allergic, respiratory diseases, wounds, etc.

3. **Ig fractions having immunomodulatory activity, *Bourel, D., Bruley-Rosset, M., Dhainaut, F., Lirochon, J.: US20056932969 (2005).***

Commentary:

The invention describes a method of preparation of Ig fractions from human polyvalent intravenous Immunoglobulin (IV Ig), which is used for the immunomodulatory effect observed during the treatment of autoimmune diseases.

4. **Identification of self and non-self antigens implicated autoimmune disease, *Strominger, J.L., Wucherpfennig, K.W.: US5874531 (1999).***

Commentary:

The present invention provides isolated peptides playing a significant role in the manifestation of autoimmune diseases such as *Pemphigus vulgaris* and multiple sclerosis, being derived from human pathogens implicated in the etiology and remissions of the disease.

5. **Benzene compound and pharmaceutical use thereof, *Fujita, T., Adachi, K., Kohara, T., Kiuchi, M., Chiba, K., Teshina, K., Mishina, T.: US5948820 (1999).***

Commentary:

This invention highlights the benzene compound having immunosuppressive effect used as an inhibitor for the rejection reaction occurring in organ or bone marrow transplantation. It is also used as a preventive or remedy for articular rheumatism, atopic eczema (dermatitis), uveal disease, systemic lupus erythematosus, Sjogren's syndrome, multiple sclerosis, myasthenia gravis, type I diabetes, endocrine ophthalmopathy, primary biliary, cirrhosis, Crohn's disease, glomerulonephritis, sarcoidosis, psoriasis, pemphigus, aplastic anemia, idiopathic thrombocytopenic purpura, allergy, polyarteritis nodosa, progressive systemic sclerosis, mixed connective-tissue disease, aortitis syndrome, polymyositis, dermatomyositis, Wegener's granuloma, ulcerative colitis, active chronic hepatitis, autoimmune hemolytic anemia, Evans' syndrome, bronchial asthma and pollinosis.