

Patent Annotations:

INHIBITORS OF EPOXIDE HYDROLASE

1. **Inhibitors of epoxide hydrolase for the treatment of hypertension**, *Kroetz, D.L., Zeldin, D.C., Hammock, B.D., Morisseau, C., US6693130 (2004)*.

Commentary:

This invention discusses the inhibitors of epoxide hydrolase that are useful for the treatment of hypertension and other inflammatory diseases such as Adult Respiratory Distress Syndrome. The compounds where R is represented by alkyl or aryl and the compounds are discussed. Methods for determining the quantity of DHET's and EET's are also described.

VASCULAR ENDOTHELIN SYSTEM IN HYPERTENSION

1. **Gene delivery compositions and methods**, *Lawrence, III, J.H., Donahue, J.K., US6855701 (2005)*.

Commentary:

The invention describes methods for enhancing vascular permeability to facilitate in the delivery of nucleic acids to the target tissues. The method also facilitates gene transfer and gene expression to heart. The method is also effective for preventing rejection of xenografts, as well as for gene therapy of tumors.

2. **Dibenzodiazepine endothelin antagonists**, *Murugesan, N., US5420123 (1995)*.

Commentary:

New endothelin antagonists i.e. oxo-dibenzodiazepine derivatives with various compositions are discussed as anti-hypertensive agents and are also used for the treatment of renal disorders associated to endotoxic shock.

3. **Method of converting big endothelin-1 to endothelin-1 with human apolipoprotein B**, *Ohwaki, T., Sakai, H., US5468623 (1995)*.

Commentary:

A method for the prevention of atherosclerosis caused by the over-secretion of the endothelin-1 with the help of apolipoprotein B. Apolipoprotein B exhibits enzyme converting property which is depicted in the conversion of big endothelin-1 to endothelin-1.

4. **Methods for determining whether an agent possesses a defined biological activity**, *Lum, P.Y., Tan, Y., Dai, H., Muise, E.S., Berger, J.P., Thompson, J.R., US20050084872A1 (2005)*.

Commentary:

The present invention compares the significance of biological activity of the candidate drug with those of existing drugs. The effectiveness is measured by comparison of the toxicity, efficacy, classifier values and result analysis

with respect to level of expression of this agent with the reference drugs.

5. **Trp-p8 active compounds and therapeutic treatment methods**, *Reynolds, M., Polakis, P., US20050090514A1 (2005)*.

Commentary:

Angiogenesis, apoptosis mediated ailments, tumors, cell-proliferation and cancer are treated with Trp-p8 active compounds. The invention discusses compounds, analogs, prodrugs, metabolites and methods used for prophylaxis and usage of contact of cancerous cells with the therapeutic amount of cool-genic compounds.

OXIDATION STRESS INHIBITOR

1. **Oxidation stress inhibitor and method of measuring oxidation stress**, *Yamamoto, Y., Takahashi, C., Watanabe, K., WO03024446A1 (2003)*.

Commentary:

Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), a strong novel free radical scavenger, is useful for the treatment of brain infarction, cerebral edema and cardiovascular diseases, stroke, vascular dementia, heart disease or myocardial infarct, diseases related to the aging, and peripheral circulatory disorders. A method for the assessment of grade of oxidative stress is described.

2. **Remedies for Amyotrophic lateral sclerosis (ALS)**, *Ikeda, K., WO0234264A1 (2002)*.

Commentary:

The present invention encompasses the usage of a novel drug edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one) and its derivatives for the treatment of motor neuron diseases, including amyotrophic lateral sclerosis.

3. **Agent for treating and/or preventing mitochondrial encephalomyopathy**, *Maeda, K., Yasuda, H., JP2005089456A2 (2005)*.

Commentary:

Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), a strong novel free radical scavenger, is useful for the treatment of mitochondrial myopathy.

CARDIOVASCULAR AGENTS

1. **Methods for identifying cardiovascular agents**, *Mendelsohn, M.E., Karas, R.H., US6692928 (2004)*.

Commentary:

The present invention provides methods for analyzing cardiovascular agents classified as vasoprotective agents, antihypertensive agents, cardiomyopathy therapeutic agents, coronary heart disease therapeutic agents, or heart failure therapeutic agents. The enzyme activity was measured by

different assays and by determining the nitric oxide synthase gene in the presence and absence of the agent.

PREVENTION OF RESTENOSIS POST-ANGIOPLASTY

1. **Composition and method for treatment and prevention of restenosis**, *Fujise, K., Mnjoyan, Z.H., US20040242470A1 (2004)*.

Commentary:

The invention features compositions, process and treatment of atherosclerosis and restenosis by a new inhibitor of smooth muscle cell proliferation comprising a soluble protein, natural or synthetic protein or biologically active region of soluble proteins. These PARIS-1 (neuronal pentraxin 1), PARIS-2 (SBP (MIC-1, GDF-15), PARIS-3 (BTG2) and PARIS-4 (soluble fractalkine) proteins also suppress proliferation of smooth muscle cells. An assay for screening mRNAs and characterization of genes encoding PARISs is also discussed.

MOLECULAR TARGETS AND CARDIAC HYPERTROPHY

1. **Calcineurin Modulators**, *Clf Medical Technology Acceleration Program, Inc., WO03006619A3 (2003)*.

Commentary:

The present invention provides compositions of Adapt78 peptides, linear peptides, cyclic peptides, peptide analogs, peptidomimetics, combinatorial chemicals and whole proteins exhibiting calcineurin modulating activity useful for treating Alzheimer's disease, cancer, hypertrophy, immune system dysfunction, or conditions characterized by calcineurin overexpression. Pathologies associated with calcineurin and adapt78 such as cardiac, brain, immune system and developmental abnormalities are treated with these peptides. Human cells and tissues are also protected against stress damage with the property of the cytoprotective activity of adapt78.

2. **Methods for screening of modulators of calcineurin activity**, *Voelkel, H., US6875581 (2005)*.

Commentary:

The present invention discusses molecular and cellular bioassays for screening modulators of calcineurin (immunosuppressive drugs) which prevent or potentiate interactions between calcineurin and CuZnSOD.

3. **Methods and compositions relating to muscle sarcomeric calcineurin-binding proteins**, *Olson, E.N., Frey, N., US20040186275A1 (2004)*.

Commentary:

The invention deal with modulating calcineurin activity by purified muscle specific sarcomeric calcineurin-binding, calcineurin associated protein (calsarcin) for the prevention of cardiac hypertrophy, heart failure or type II diabetes.

4. **Methods for preventing cardiac hypertrophy and failure by inhibition of MEF2 transcription factor inhibitor**, *Olson, E.N., US2002010069A1 (2002)*.

Commentary:

The present invention features involvement of molecular events in the treatment of cardiac hypertrophy and also relates to process of transgenic constructs for preparing transgenic animals. The inhibition of the transcription factor myocyte enhancer factor-2 and Ca⁺⁺ stimulation of the hypertrophic response are mediated through MEF2.

5. **Inhibition of histone deacetylase as a treatment for cardiac hypertrophy**, *Long, C., Olson, E.N., Bristow, M.R., McKinsey, T.A., US6706686 (2004), US20040186049A1 (2004) and EP1297851B1 (2005)*.

Commentary:

Cardiac hypertrophy and heart failure are treated by Class II HDACs inhibitors by a mechanism involving inhibition of fetal cardiac gene expression and interference with sarcomeric organization.

6. **HDAC4 and HDAC5 in the regulation of cardiac gene expression**, *Olson, E.N., Lu, J., McKinsey, T.A., WO0114581C2, WO0114581A2 (2002) and WO0114581A3 (2002)*.

Commentary:

The invention features composition, characterization and molecular procedures of inhibitor of cardiac hypertrophy for treating cardiac hypertrophy by interaction of HDAC 4 and 5 with MEF2. The identification of compounds possessing inhibition activity against cardiac hypertrophy is also discussed.

7. **Inhibition of histone deacetylase as treatment for cardiac hypertrophy**, *Olson, E.N., McKinsey, T.A., Bristow, M.R., Long, C., JP2003238445A2 (2003)*.

Commentary:

Pathological cardiac hypertrophy and heart failure are prevented by subjecting the patient to histone deacetylase inhibitor that acts by inhibiting a fetal cardiac gene expression of an embryo.

8. **Inhibition of protein kinase C-MU (PKD) as a treatment for cardiac hypertrophy and heart failure**, *McKinsey, T.A., Olson, E.N., Vega, R.B., WO04112763A2 (2004) and WO04112763A3 (2004)*.

Commentary:

The present invention describes a method for inhibition of Protein Kinase D for preventing pathological cardiac hypertrophy and heart failure. The link between MEF-2 and Class II HDAC's and a kinase known as PKD MEF-2 and Class II HDAC's is also presented. The role of inhibitors of PKD for partially inhibiting the fetal cardiac gene expression and cellular reorganization when MEF-2 dependent transcription is inhibited, is also elaborated.

9. **Carbamic acid compounds comprising a bicyclic heteroaryl group as HDAC inhibitors**, *Finn, P.W., Kalvinsh, I., Loza, E., Andrianov, V., Habarova, O., Lolya, D., Piskunova, I., WO04076386A3 (2004)*.

Commentary:

The present invention related to formulations of carbamic acid compounds, which act as histone deacetylase HDAC inhibitors and are used both *in vitro* and *in vivo* for the cure of cancer, proliferative conditions, psoriasis, atherosclerosis, Alzheimer's disease and rheumatoid arthritis.

STEROL ABSORPTION INHIBITOR(S)

1. **Combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions, Kosoglou, T., Veltri, E.P., Ress, R.J., Strony, J., Hauer, W., CA2434436AA (2002).**

Commentary:

The method, compositions and combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions are discussed. These formulations are also used for the treatment of obesity, diabetes and lowering plasma levels of sterols.

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AND TORCETRAPIB

1. **Substituted heterocyclic derivatives useful as anti-diabetic and antiobesity agents and method, Cheng, P.T.W., Chen, S., Ding, C.Z., Herpin, T.F., US6875782 (2005).**

Commentary:

The invention features treatment of diabetes, obesity and various epithelial tumors with substituted heterocyclic derivatives.

2. **Substituted tertiary-heteroalkyl-amines useful for inhibiting cholesteryl ester transfer protein activity, Sikorski, J.A., Durley, R.C., Rueppel, M.L., Mischke, D.A., Parnas, B.L., US6924313 (2005).**

Commentary:

The invention provides details of administering substituted tertiary-heteroalkylamine compounds to mammals for the treatment of atherosclerosis hyperlipidemia, stroke and coronary artery disease.

3. **Combinations of cholesteryl ester transfer protein inhibitors and nicotinic acid derivatives for cardiovascular indications, Sikoski, J.A., Glen, K.C., US6890958 (2005).**

Commentary:

The invention describes formulations of combination therapy for the prevention of hypercholesterolemia, hyperlipidemia and atherosclerosis with initial dose of nicotinic acid derivative compound followed by subsequent dose of cholesteryl ester transfer protein inhibiting compound.