Title: Nox4 Small Molecule Inhibitors for the Treatment of Fibrotic Disorders

Invention: This technology identifies a series of small molecule inhibitors of NOX4 for the treatment of idiopathic pulmonary fibrosis (IPF) and other fibrotic disorders. In particular, it provides methods, screening assays, and related absorption, distribution, metabolism, excretion (ADME) studies for the disclosed compounds. This invention explores the impaired response to cellular oxidative stress as a core pathway to organ fibrosis.

Background: Fibrosis is the development of excess connective tissue due to the activation of myofibroblasts. It is a key process in the pathophysiology of conditions such as lung injury and kidney disease. Members of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) family catalyze the formation of reactive oxygen species and ROS-forming enzyme, NOX4, and have shown to be a critical mediator of myofibroblast differentiation in lung injury, thereby supporting tissue fibrogenesis. This technology provides a series of novel NOX4-specific inhibitors for the therapeutic treatment of IPF and other fibrotic disorders.

Applications:
- Fulfills the market gap for anti-fibrotic drugs
- An "orphan disease" can be extremely attractive in the strategic development of moving a drug to market
- In addition to all other pharmacochemical properties the IC50 of the lead compounds is comparable to the GKT NOX1/4 inhibitor in the low to sub micro molar range, implying that these compounds have great potential for clinical translation

Advantages:
- Addresses the unmet need for IPF drug therapies
- This is the first research group to identify NADPH oxidase NOX4 as a mediator of myofibroblast activation
- This is the first research group to validate the role of NADPH oxidase NOX4 in animal models of lung fibrosis
- Permeability, solubility, and metabolic stability proved favorable for in vitro ADME
- Targets oxidative stress responses in myofibroblasts

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