"NOVEL INHIBITORS OF INFLAMMASOME"

VCU #13-031

Applications

- Acute myocardial infarction and ischemia
- Diabetes
- Cancer
- Gout and auto-inflammatory diseases

Advantages

- Lower toxicity due to low doses
- Better solubility
- Wide range of applications

Inventors

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Market Need

Acute myocardial infarction (AMI) is among the most causes of adverse cardiac remodeling, heart failure, and death worldwide. Cryopyrin has been shown to play a major role in the formation of the inflammasome in the heart during AIM and its potential inhibitors could be used to prevent adverse cardiac remodeling after AIM. There is an urgent need for new therapeutic strategies specifically aimed at modulating inflammation during AIM. The current approach of reperfusion and inhibition of neurohormonal activation has successfully reduced morbidity and mortality of AIM, but is still associated with unacceptably high incidence of heart failure and death that may be related to the excessive inflammatory activity. Glyburide is an anti-diabetic drug shown to also inhibit cryopyrin, but the need for high doses causes severe hypoglycemia and has been shown to be cardiotoxic.

Technology Summary

This invention presents a new class of anti-inflammatory drugs and their potential to limit cardiac injury due to a sterile inflammation during AIM and prevent heart failure through inhibition of the cryopyrin inflammasome. Dr. Abbate and colleagues from Virginia Commonwealth University have designed and investigated several glyburide analogs that are chemically stable, show lower toxicity, and specifically inhibit cryopyrin inflammasome. Figure below demonstrates one of the compound (GA2) inhibiting activity. Such inflammasome inhibitors may prove useful not only for treatment of AIM, but also in other inflammasome-mediated diseases such as diabetes, gout, and auto-inflammatory diseases.

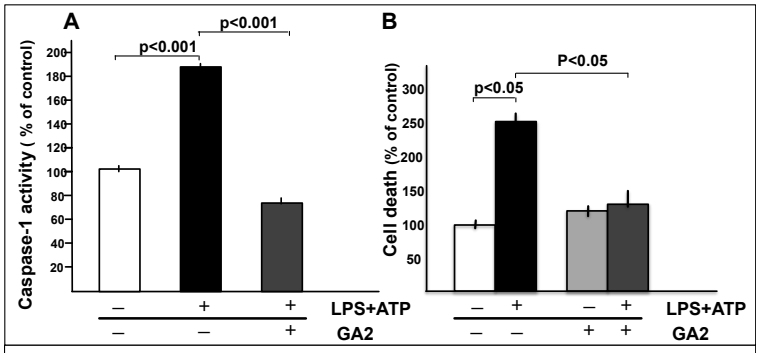

Figure 6. Caspase-1 activity (A) and cell death [Trypan Blue Exclusion Assay](B) after LPS+ATP stimulation without and with the addition of compound GA2.

Technology Status

In vitro and *in vivo* data available.
Patent pending: U.S. and foreign rights available

This technology is available for licensing to industry for further development and commercialization.