Selective Antagonists of the RIG-I Innate Immune Receptor

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RIG-I: a promising new drug target

- Antiviral Response
- Viral Protection
- Antitumor therapy
- Dysregulated inflammation

Our Innate Immune Sensor
For Viral RNA
The Market for RIG-I Antagonists

RIG-I Hyperactivation

- COPD morbidity
- Sjogren’s syndrome, autoimmunity
- Acute radiation toxicity
- Oligo therapeutic toxicity (miRNA)

- Market value for COPD alone: $14B by 2025
Caught in the act: The RIG-I innate immune receptor bound to target RNA

The Pyle Laboratory completed the structural and biochemical studies needed for elucidating RIG-I activation mechanism and developing HTS assays. Iwasaki Lab provides in-vivo methodology and experimental design.
Pilot Studies – proof of concept

- **Pilot Screen** of 10,000 curated compounds → antagonist hit with IC$_{50}$ of 8 µM
- **SAR, limited optimization** → RIG012 with IC$_{50}$ of 0.7 µM

*Inhibition in-vitro*  
*Selective inhibition in cells*

*This sets the stage for large-scale HTS and lead optimization*
Next Steps:

Using our assay platforms and crystal structures...

- Large scale HTS with experienced CRO specialists
- Deduce preliminary SAR from screening data
- Conduct initial lead optimization on promising hits
- Initial optimization of pharmacological properties
Seed Funding:

Seed Series:  $800,000

- HTS study and CRO contract
- Preliminary Medicinal Chemistry
- CSO: Medicinal Chemist
- CEO: Drug Development Entrepreneur