

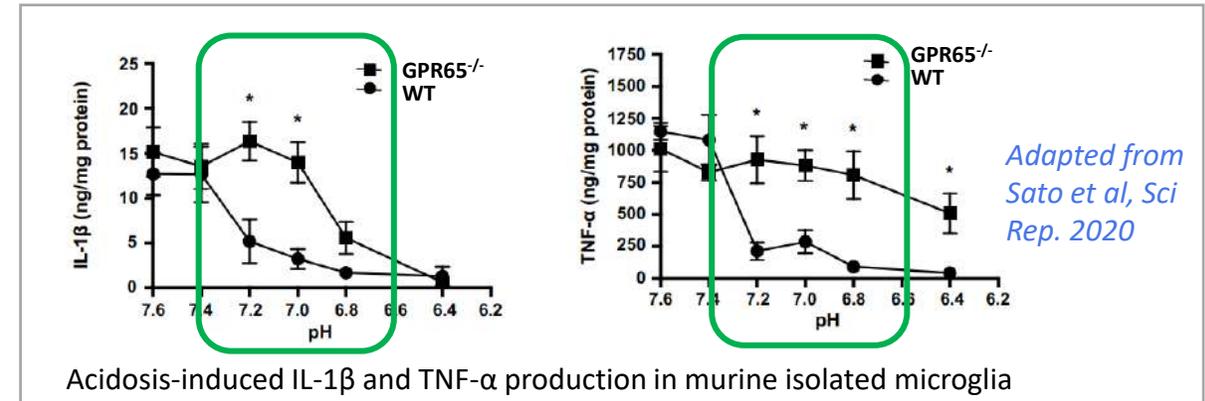
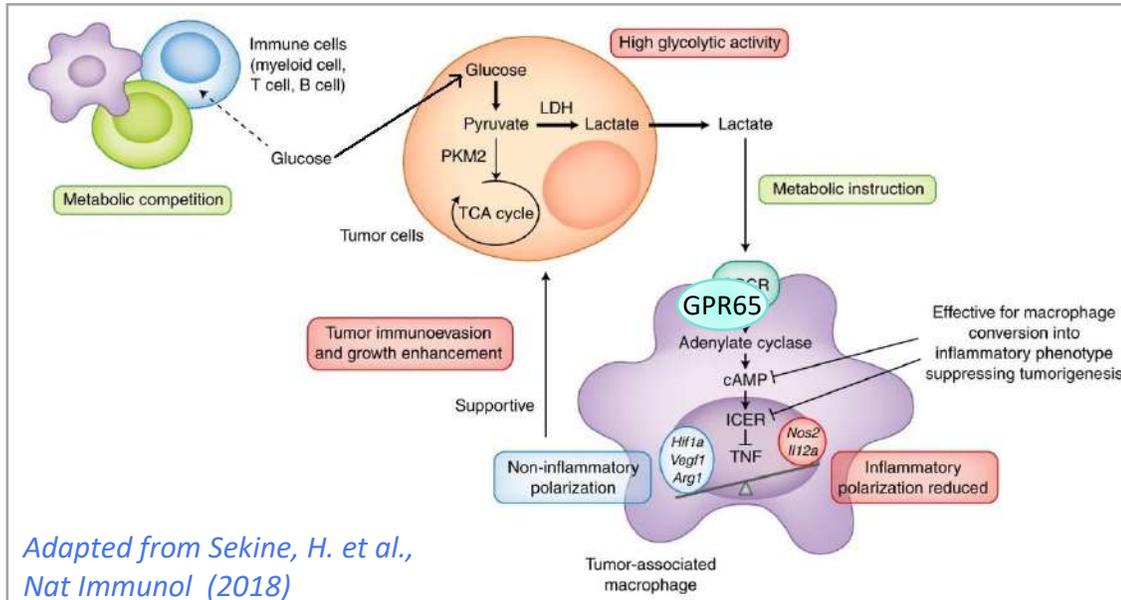
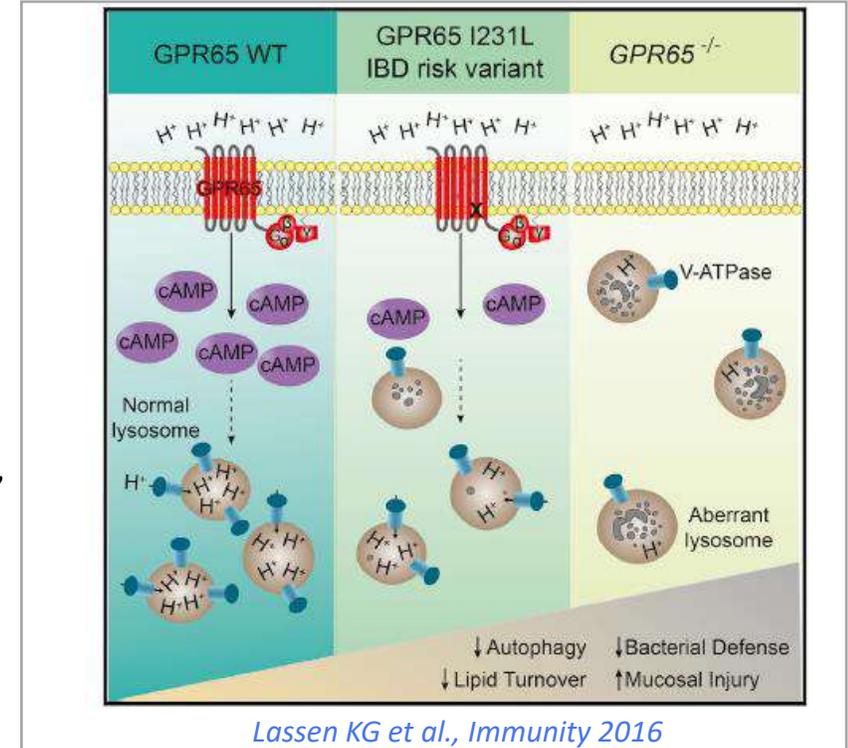
## GPR65 Modulators

*Nonconfidential*

**lead:pro**

# GPR65 Modulators Program

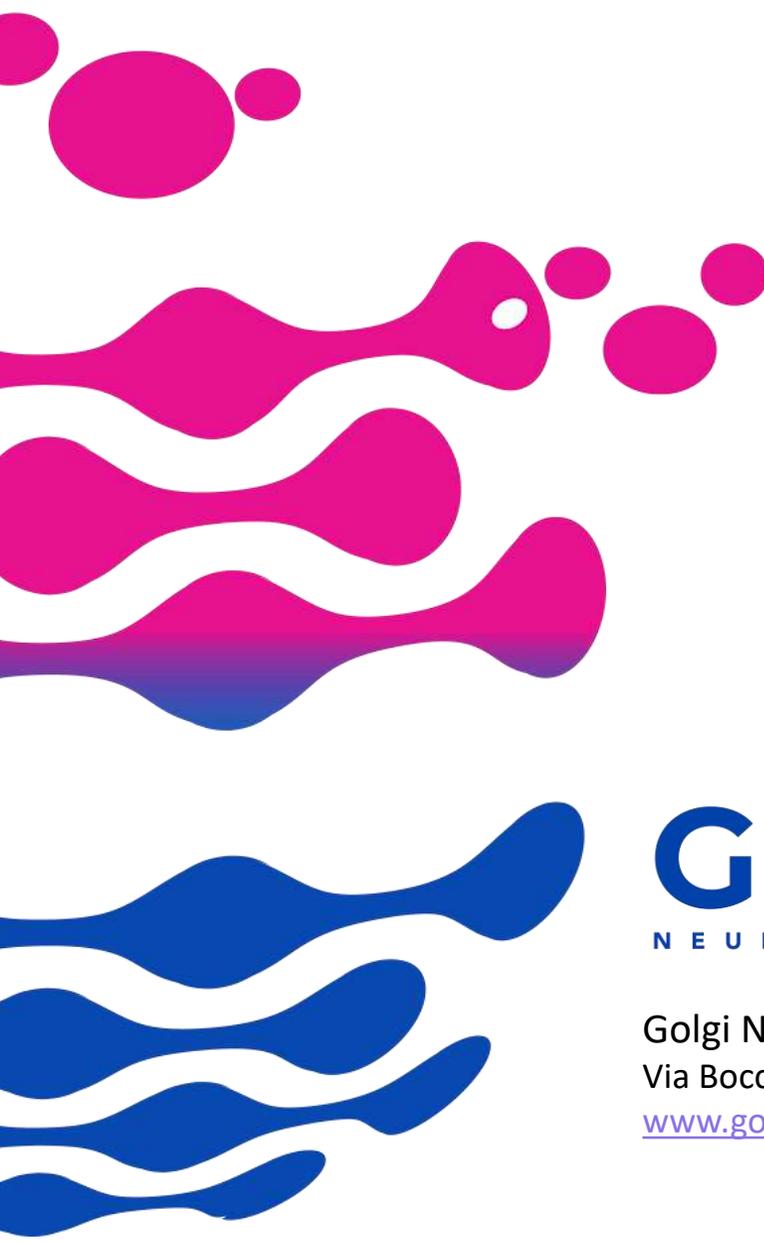
- GPR65 is a Gas-coupled **GPCR** **activated by acidic pH** and expressed in immune cells, such as tumor-associated macrophages and microglia
- Several polymorphisms in GPR65 have been associated with chronic inflammatory diseases, autoimmune diseases and multiple cancers. A **hypomorphic variant (I231L)** correlates with inflammatory bowel disease and improved survival in cancer patients
- GPR65 activation leads to **reduction of inflammatory immune response**, regulates **lysosomal functionality** and could be protective or detrimental based on the disease model
- **Indications:** neuroinflammation, inflammatory bowel disease, atopic dermatitis, asthma, immuno-oncology, autoimmune diseases, multiple sclerosis, Parkinson's disease, fibrosis



# GPR65 Modulators Program – Executive Summary

<b>Status</b>	<ul style="list-style-type: none"><li>➤ Positive and negative small molecule modulators identified by HTS, several hit classes</li><li>➤ 3 series in Lead Generation</li><li>➤ GPR65 G<math>\alpha</math>-protein complex cryo-EM structure available</li></ul>
<b>Strengths</b>	<ul style="list-style-type: none"><li>➤ <b>The first available Cryo-EM structure of GPR65 could effectively guide Lead generation</b></li></ul>
<b>Assets</b>	<ul style="list-style-type: none"><li>➤ Qualified positive and negative GPR65 modulators, initial SAR established</li><li>➤ Cellular assays and Biophysical binding assays available for the screening funnel</li><li>➤ Structural information to enable structure-based drug design</li><li>➤ Cryo-EM structure of GPR65-G<math>\alpha</math>-protein complex</li></ul>
<b>Competition</b>	<ul style="list-style-type: none"><li>➤ No positive small molecule modulators are described in public databases</li><li>➤ Few small molecule antagonists are in development (preclinical stage)</li></ul>

- **Program developable for both positive and negative modulators, available for partnership**



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