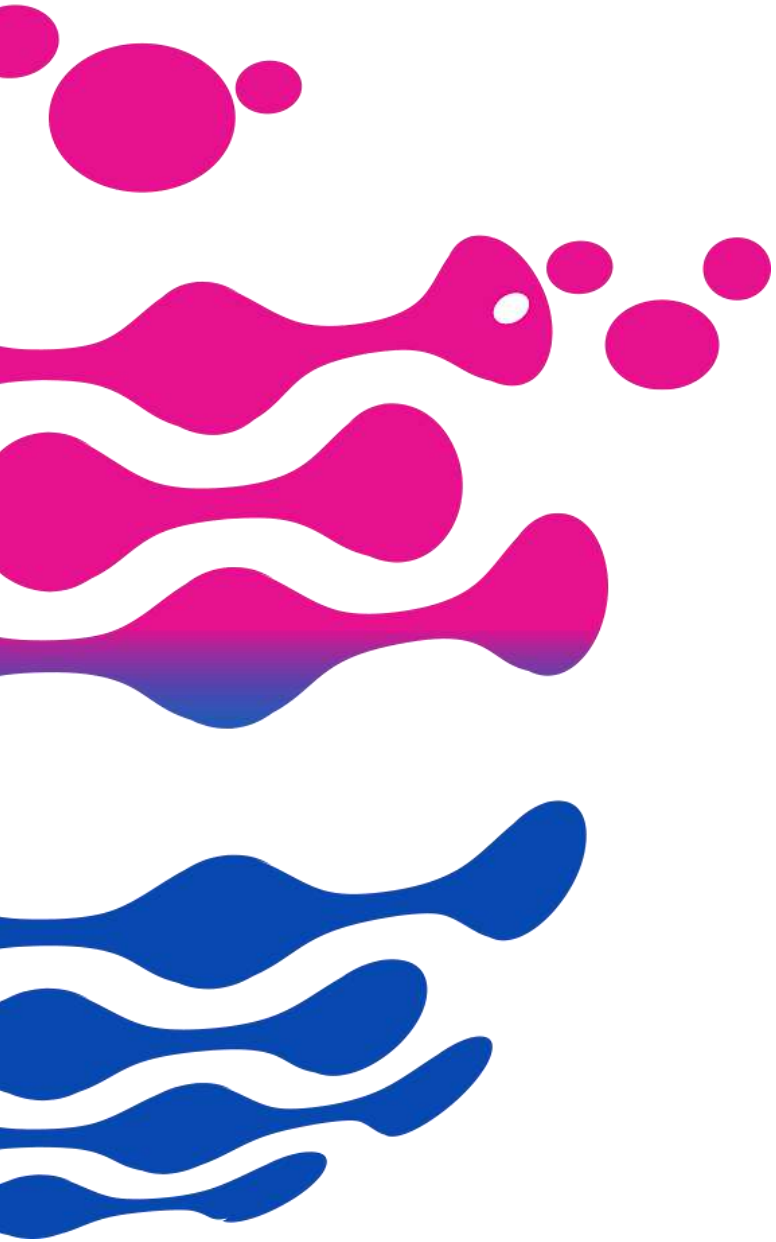


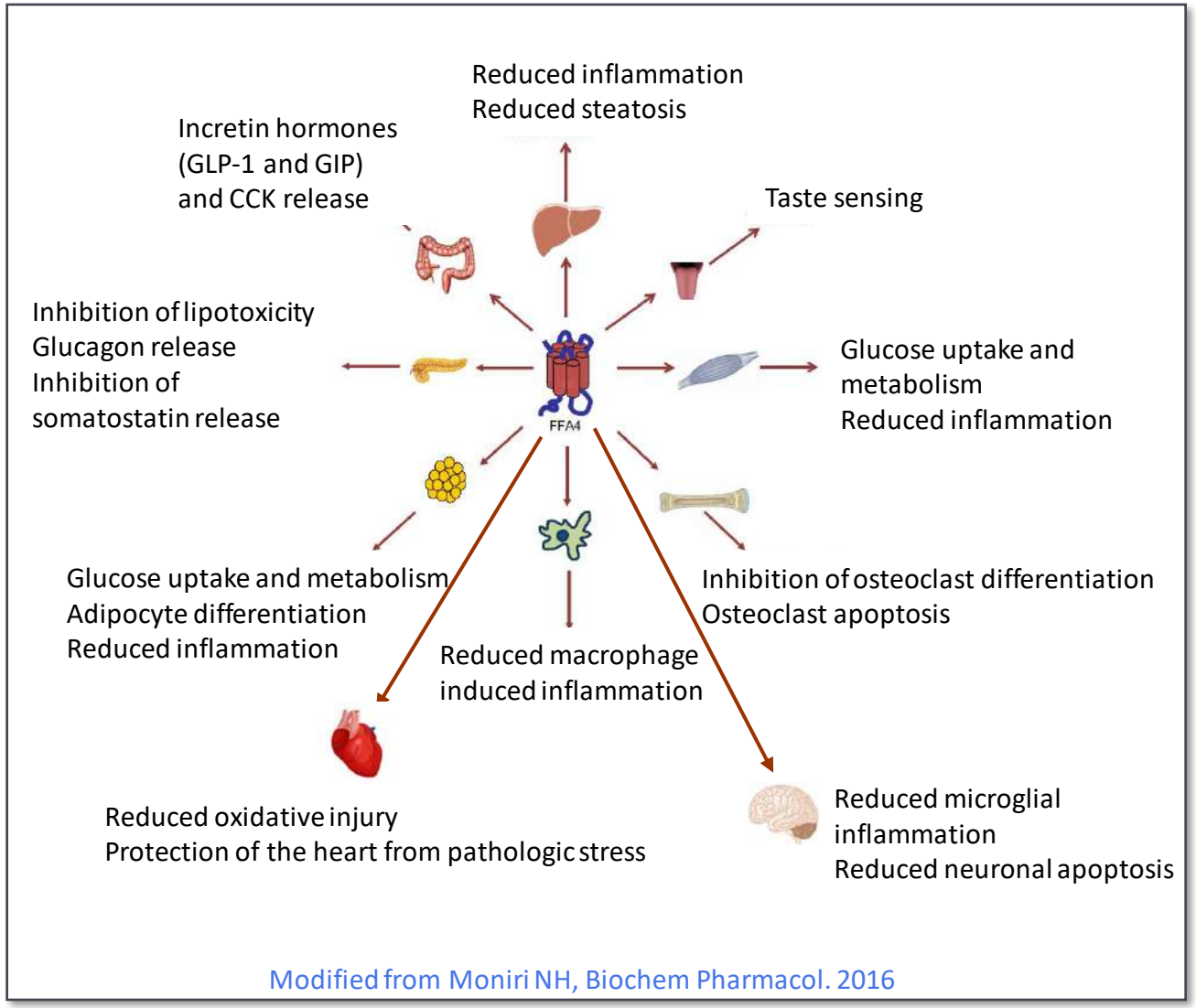
GOLGI NEUROSCIENCES

GPR120 Agonists

Nonconfidential

GPR120 Agonists Program

- GPR120 is a Gαq-coupled **GPCR activated by long-chain free fatty acids** (FFAs) **such as omega-3 (ω3) FAs**; expressed in enteroendocrine cells, adipocytes, bone cells, pancreatic cells, epithelial lung cells, macrophages/microglia, etc.
- A **loss of function polymorphism** has been associated to obesity, fatty liver disease and worse cardiac outcomes
- GPR120 maintains metabolic homeostasis by promoting **GLP-1 release**, regulating insulin secretion and sensitivity in mice, adipogenesis and adipocyte metabolism, liver steatosis, peripheral and central inflammation. GPR120 appears to be the mean **mediator of the beneficial effects of ω3-fatty acids**
- **Indications:**
  - **Peripheral**: Type 2 diabetes, obesity, cardiovascular diseases, atherosclerosis, pulmonary diseases, liver injury, fibrosis
  - **CNS**: obesity - food intake, acute and chronic inflammation, epilepsy, metabolic syndrome-associated cognitive decline



Modified from Moniri NH, Biochem Pharmacol. 2016

GPR120 Agonists Program – Executive Summary

Status	➢ Agonists identified by HTS and developed ➢ **2 classes in Lead Optimization**: high activity/selectivity vs GPR40, good IP and possibility of expansion: • Class B, more advanced - good ADME, acceptable PK, oral bioavailability, CNS penetration; Lead compounds show activity in preliminary *in vitro* POC (reduction of LPS-induced IL1β release) and *in vivo* POC (acute model, reduction of food intake); patent draft application prepared • Class A, less advanced - high potency, ADME to be optimized; patent protected (WO2019175152, granted in US)
Strengths	➢ Our compounds do not have a carboxylic group/bioisostere, in contrast to most of the agonists from competition ➢ This makes them, in principle, suitable for CNS application. BBB penetration shown for one class
Assets	➢ Proprietary, orally available and BBB permeable small-molecule lead-candidate activating GPR120 ➢ Assays for the screening funnel available ➢ Computer-Aided Drug Discovery feasible (Cryo-EM solved and mode of activation determined)
Competition	➢ Other companies involved in GPR120 research include BMS, JNJ, MSD, AZ, GSK, LG Chem, etc.

➢ **Program developable for both peripheral and CNS applications, available for partnership**

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