SELECTED OPPORTUNITIES IN METABOLISM

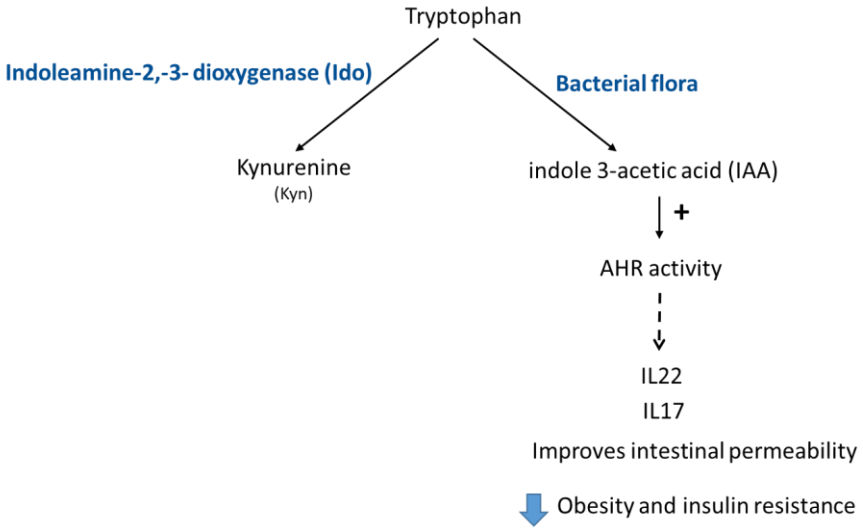
METHOD FOR PROGNOSING AND TREATING METABOLIC DISEASES (BIO17039)

BIO 17039 - METHOD FOR PROGNOSING AND TREATING METABOLIC DISEASES

Product factsheet

In vivo PoC

- **Target:**
  - Tryptophan metabolism
- **Product:**
  - IL-22 producing microbiota
- **Application:**
  - Metabolic disease
- **Technology:**
  - Probiotic



- **Rational / POC:**
  - Obesity is associated with an increase of intestinal indoleamine 2-3 dioxygenase (IDO) activity, which shifts tryptophan (Trp) metabolism from indole derivative but also IL-22 production towards kynurenine (Kyn) production;
  - The beneficial effects previously showed are due to rewiring of Trp metabolism towards a microbiota-dependent production of IL-22;
- **Patent and publication:**
  - PCT/EP2019/054946: METHODS FOR PROGNOSING AND TREATING METABOLIC DISEASES
  - Genetic deficiency of indoleamine 2,3-dioxygenase promotes gut microbiota-mediated metabolic health. Laurans L et al., Nat Med, 2018

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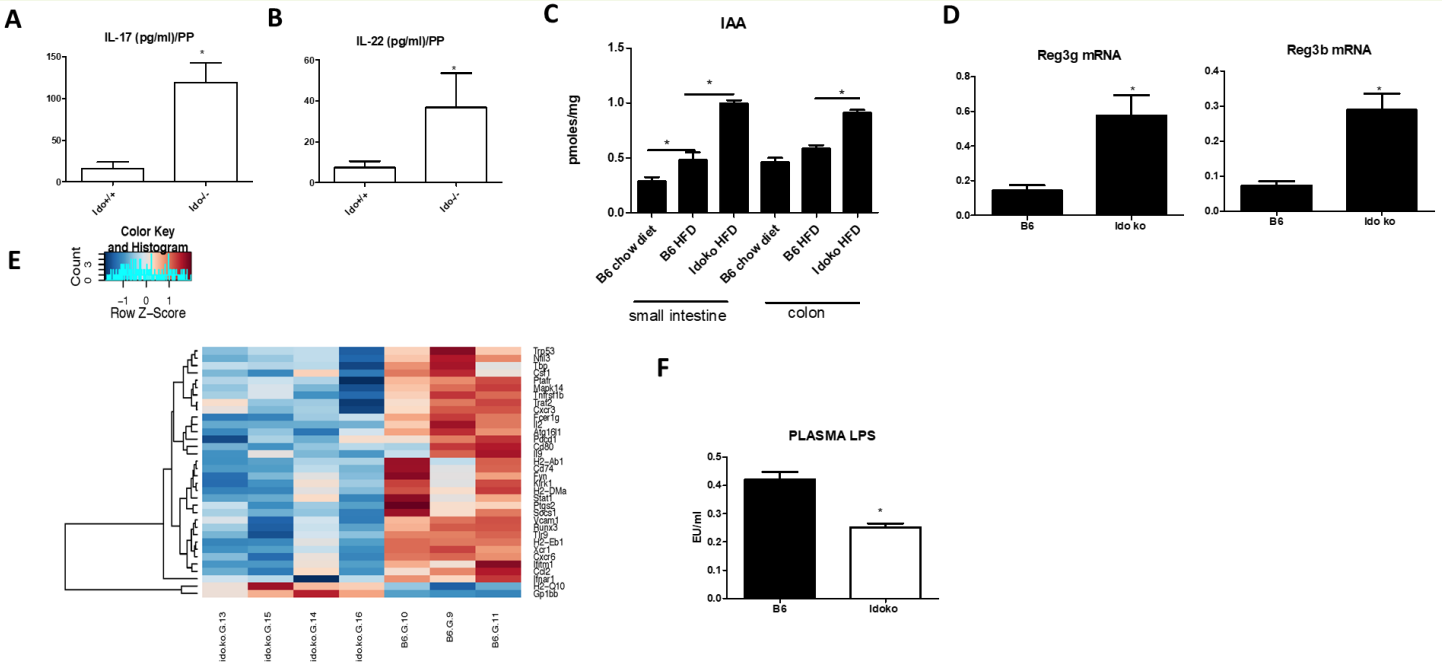
Proof of concept

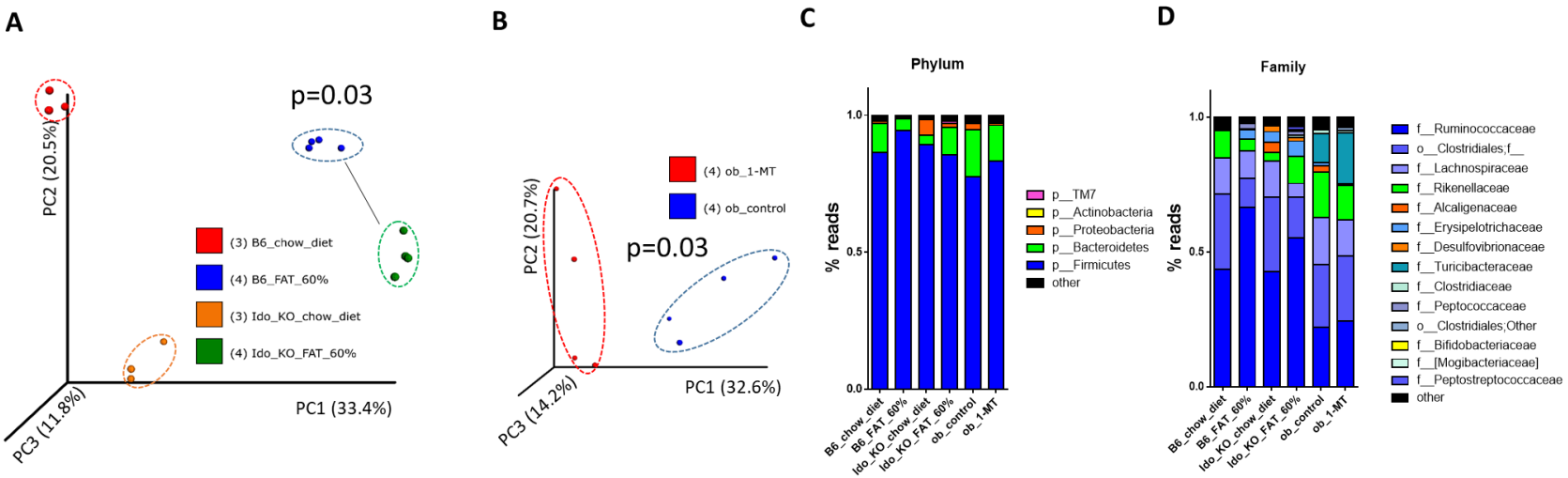
IDO deletion improves intestinal permeability in obesity context



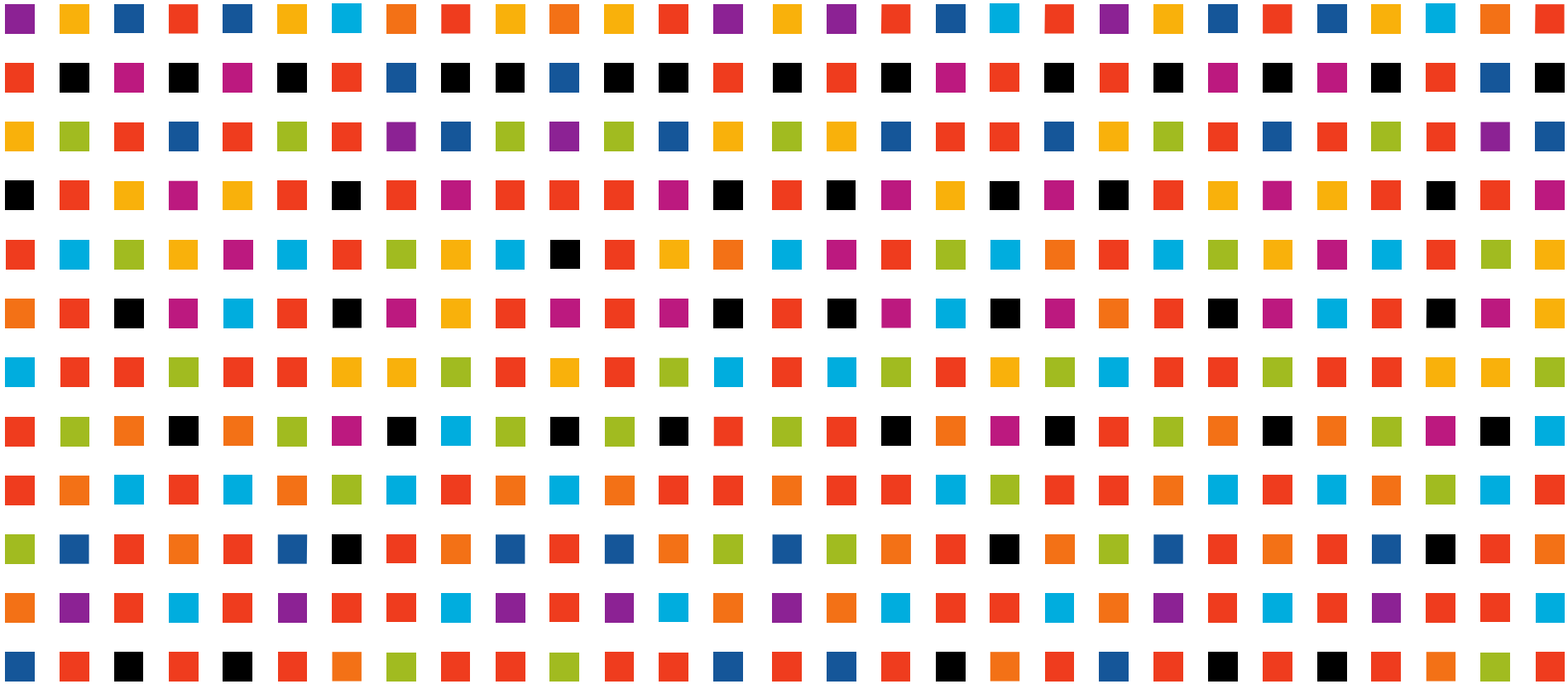
A-B IDO deletion increases the levels of IL-17 and IL-22 proteins measured by ELISA in peyer patches (PP) extracts (HFD during 7 weeks). **C** the HFD increases at a higher level in Ido ko mice fed with HFD, the production of indole 3-acetic acid (IAA), known to be Aryl hydrocarbon receptor (Ahr) agonist, in both small intestines and colons. **D** increase in intestines of Ido ko mice fed with HFD the expression (mRNA) of antimicrobial proteins (Reg3b and 3g) known to be induced by IL-22. The results show an increase, in the gastrointestinal tract of Idoko mice, the expression IL-22, IL-17, IAA and antimicrobial proteins all known to improve intestinal permeability. **E** Heat map of the gene expression of inflammatory factors which are differentially expressed in intestines of Bl6 and Idoko fed with HFD using Nanostring. The results show that the majority of inflammatory genes are down-regulated in Idoko intestines in the context of obesity. **F** IDO deletion improves intestinal permeability after 20 weeks of HFD diet as assessed by a significant decrease of plasma LPS concentration.

Proof of concept

IDO deletion or inhibition changes bacterial microbiota in obesity context



A principal component analysis (PCA) based on bacterial gene sequence abundance in feces of Bl6 and Idoko mice on either chow or high fat diet (60 % FAT) . **B** principal component analysis (PCA) based on bacterial gene sequence abundance in feces of ob/ob mice treated or not with IDO inhibitor (1 methyl tryptophan, 1MT). **C-D** bacterial taxon based analysis at phylum and family levels in the feces of Bl6 and Idoko mice or ob/ob mice treated or not with 1MT. The results show major differences in bacterial composition between bl6 and Idoko mice fed with HFD and between ob/ob mice and ob/ob mice treated with 1MT.



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