

Engineered inulin gel formulation for gut microbiota modulation and immunotherapy

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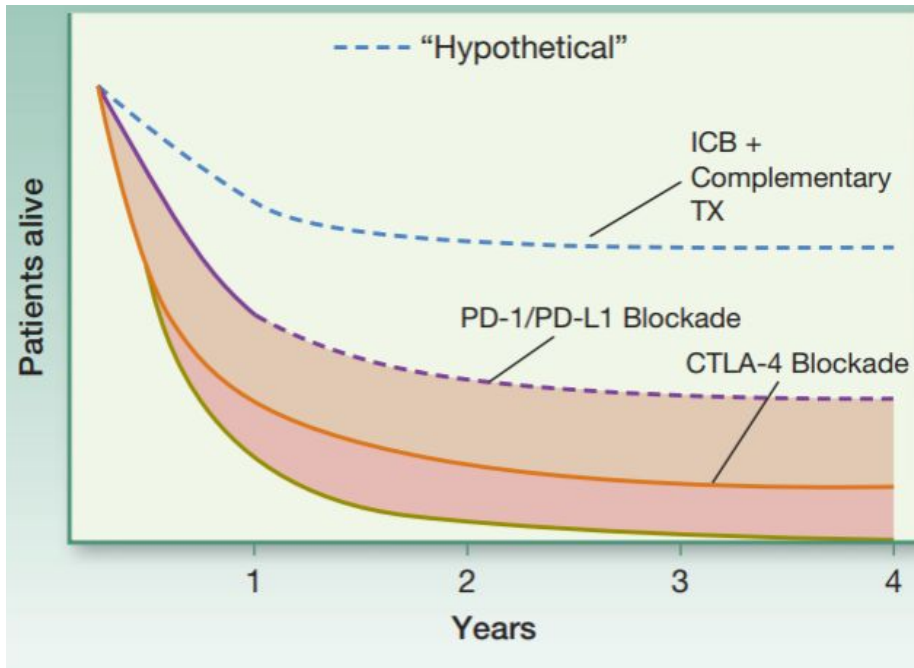
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Immunotherapy & Gut microbiota



Ott et al., *Clin. Cancer Res.* 2013, 19, 5300

CANCER IMMUNOTHERAPY

The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients

Matson et al., *Science* 2018, 359, 104

CANCER IMMUNOTHERAPY

Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients

Gopalakrishnan et al., *Science* 2018, 359, 97

CANCER IMMUNOTHERAPY

Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors

Routy et al., *Science* 2018, 359, 91



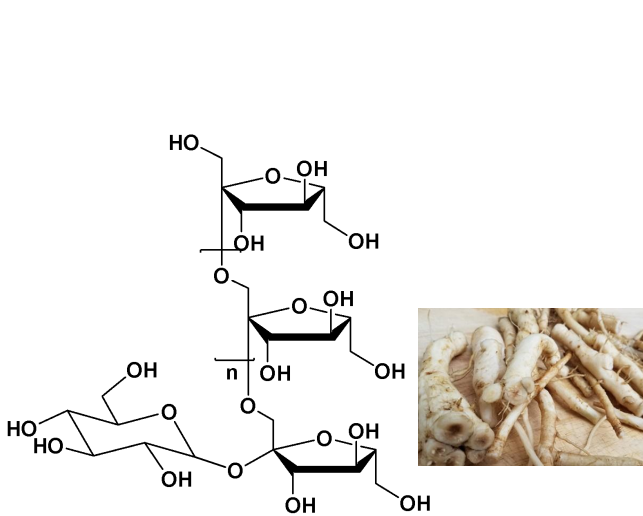
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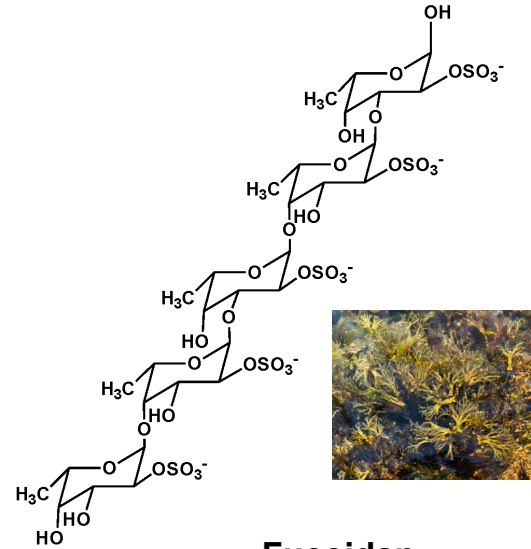


Candidates in our study



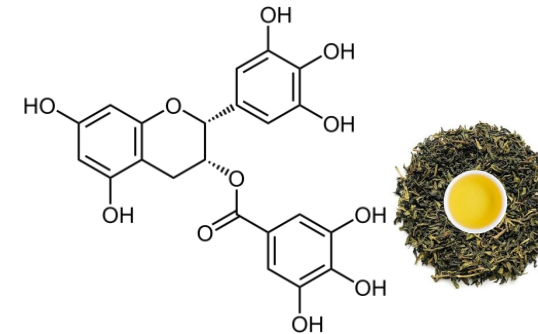
Inulin (dietary fiber)
Fructooligosaccharides
(FOS, short-chain inulin)

Vandeputte *et al.*, *Gut* 2017, 66, 1968
Smith *et al.* *BMC Microbiol.* 2019, 19, 130



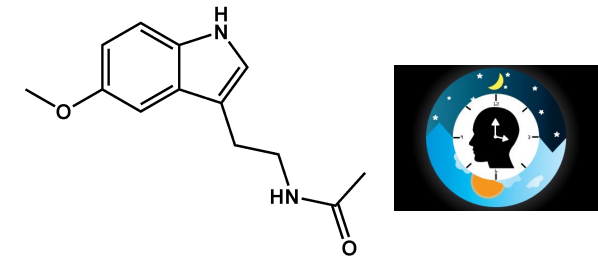
Fucoidan
(dietary fiber)

Sichert *et al.*, *Nat. Microbiol.* 2020, 25, 1
Xue *et al.*, *Food Funct.* 2018, 9, 1214



Epigallocatechin gallate
(EGCG, polyphenol, antioxidant)

Duda-Chodak *et al.*, *Eur. J. Nutr.* 2015, 54, 325
Kang *et al.*, *Cancer Res.* 2007, 67, 802



Melatonin
(drug)

Yin *et al.*, *J. Pineal Res.* 2018, 65, e12524
Ren *et al.*, *J. Pineal Res.* 2018, 64, e12448

Han *et al.*, *Nat. Biomed. Eng.*, 2021, 5, 1377-1388

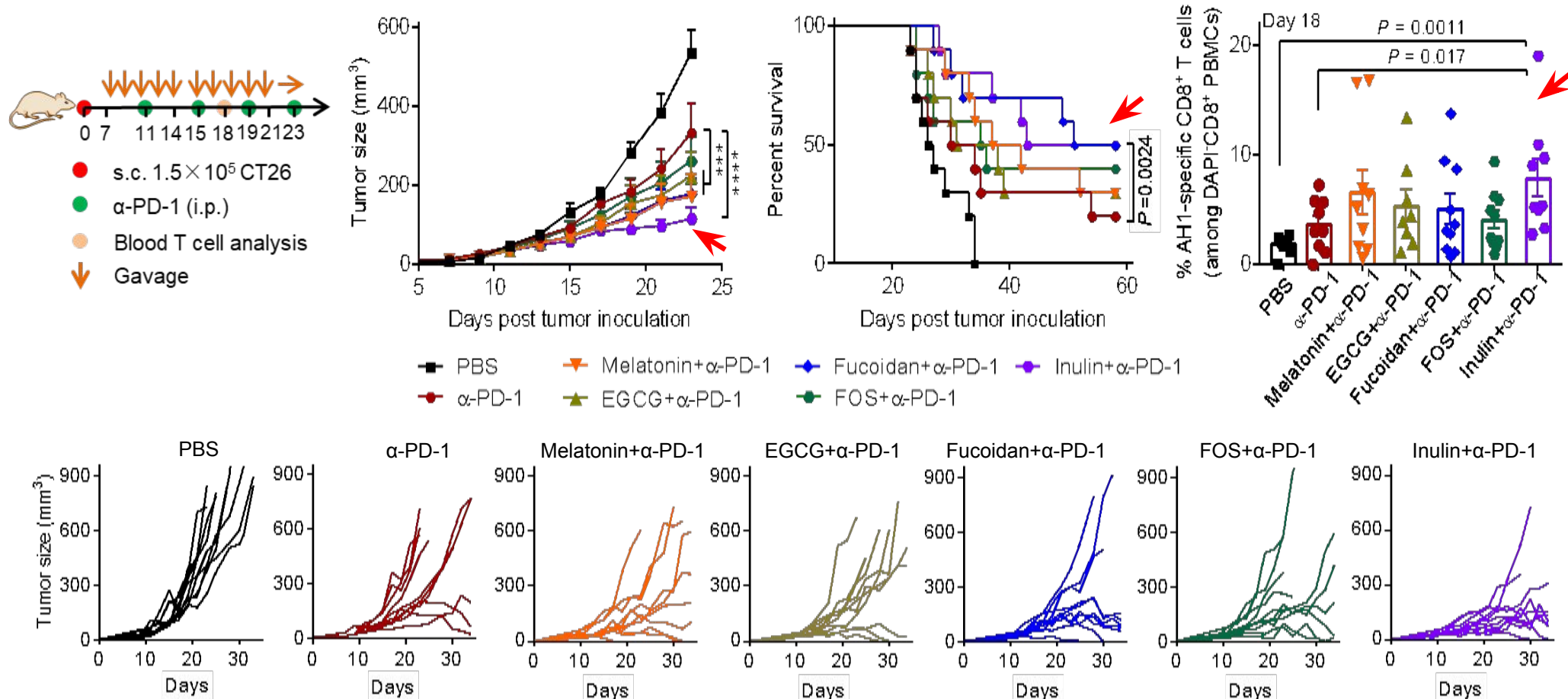


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Inulin diet synergizes with anti-PD-1 therapy given IP



Han et al., *Nat. Biomed. Eng.*, 2021, 5, 1377-1388



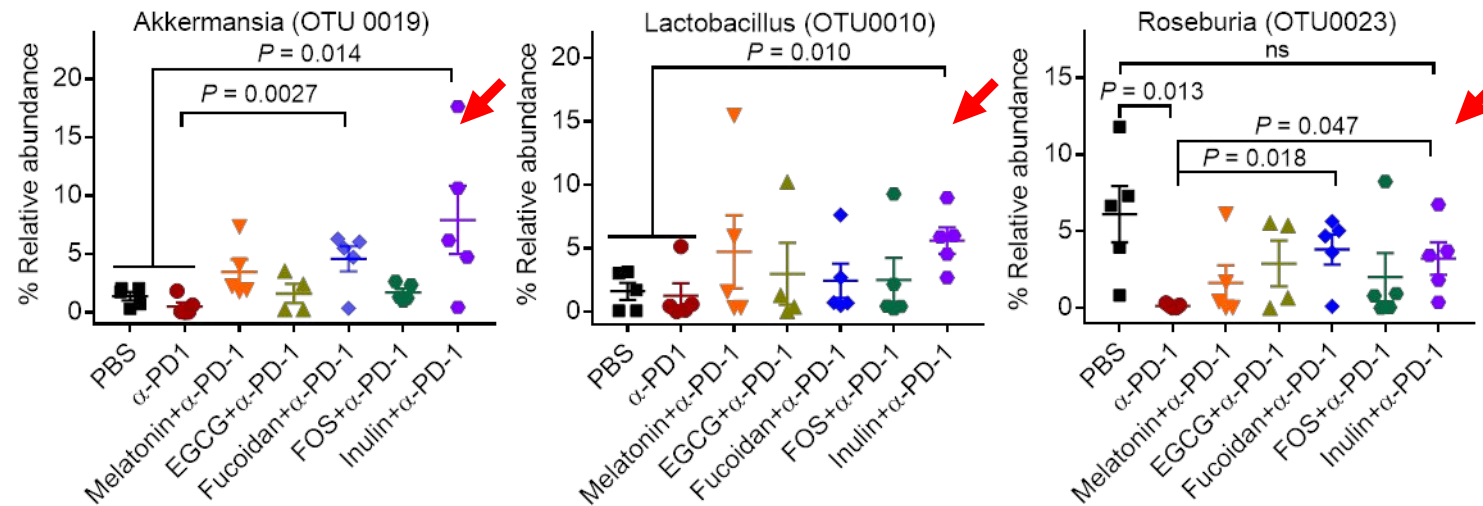
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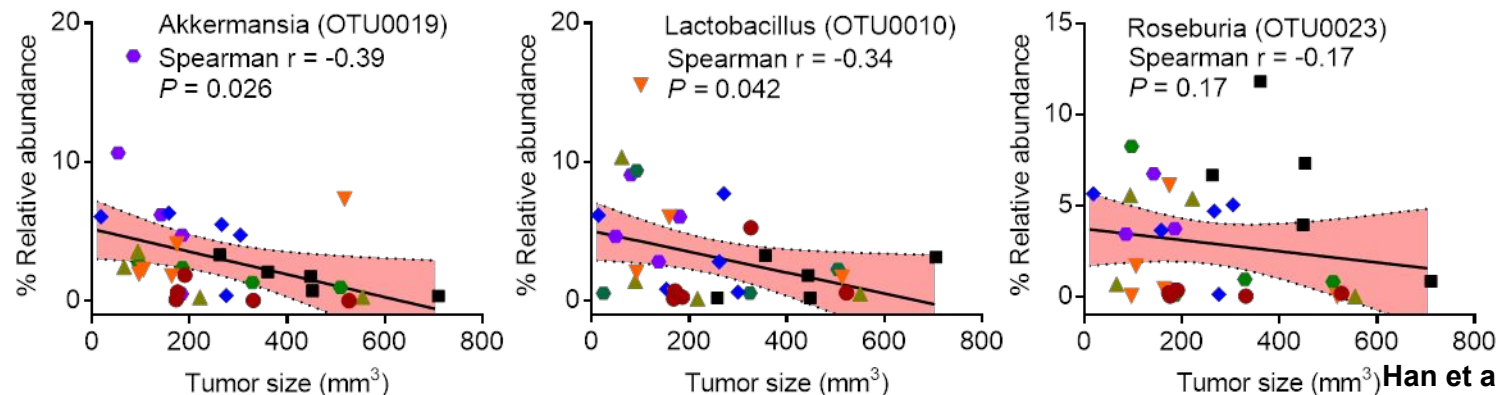
Inulin promotes “beneficial” gut microbes, which are inversely correlated with tumor growth

Microbes abundances



Routy et al., *Science* 2018, 359, 91
Matson et al., *Science* 2018, 359, 104

Spearman's correlation analysis



Han et al., *Nat. Biomed. Eng.*, 2021, 5, 1377-1388



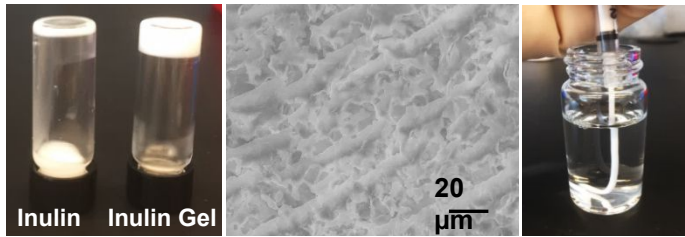
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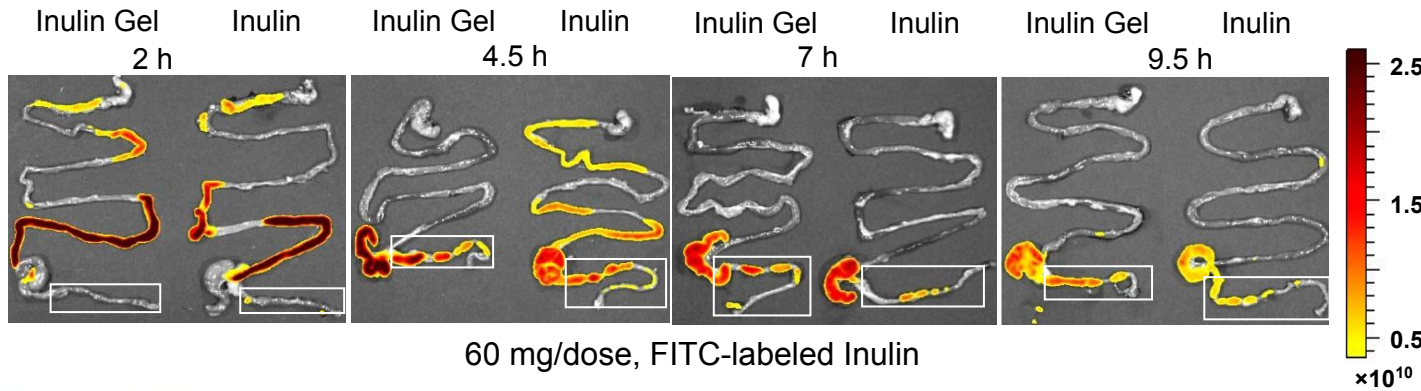
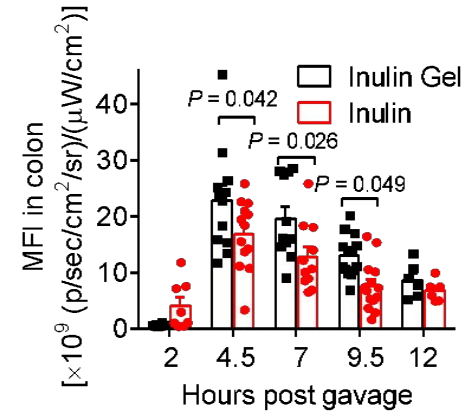
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Engineered inulin hydrogel with prolonged colon retention modulates the gut microbiota

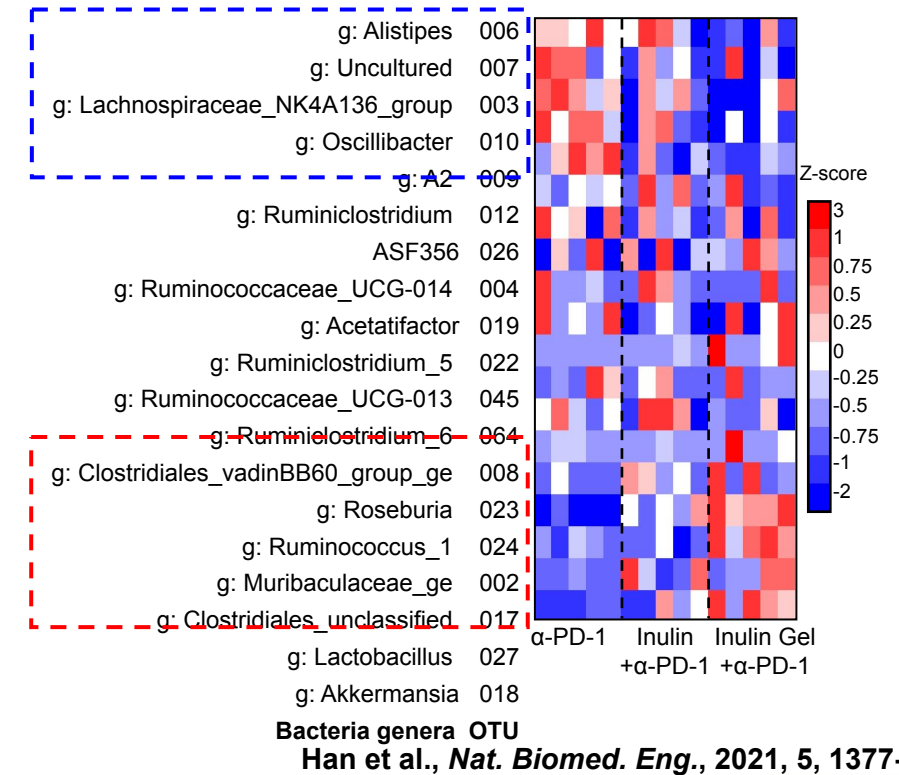
Injectable inulin hydrogel



Prolonged colon retention

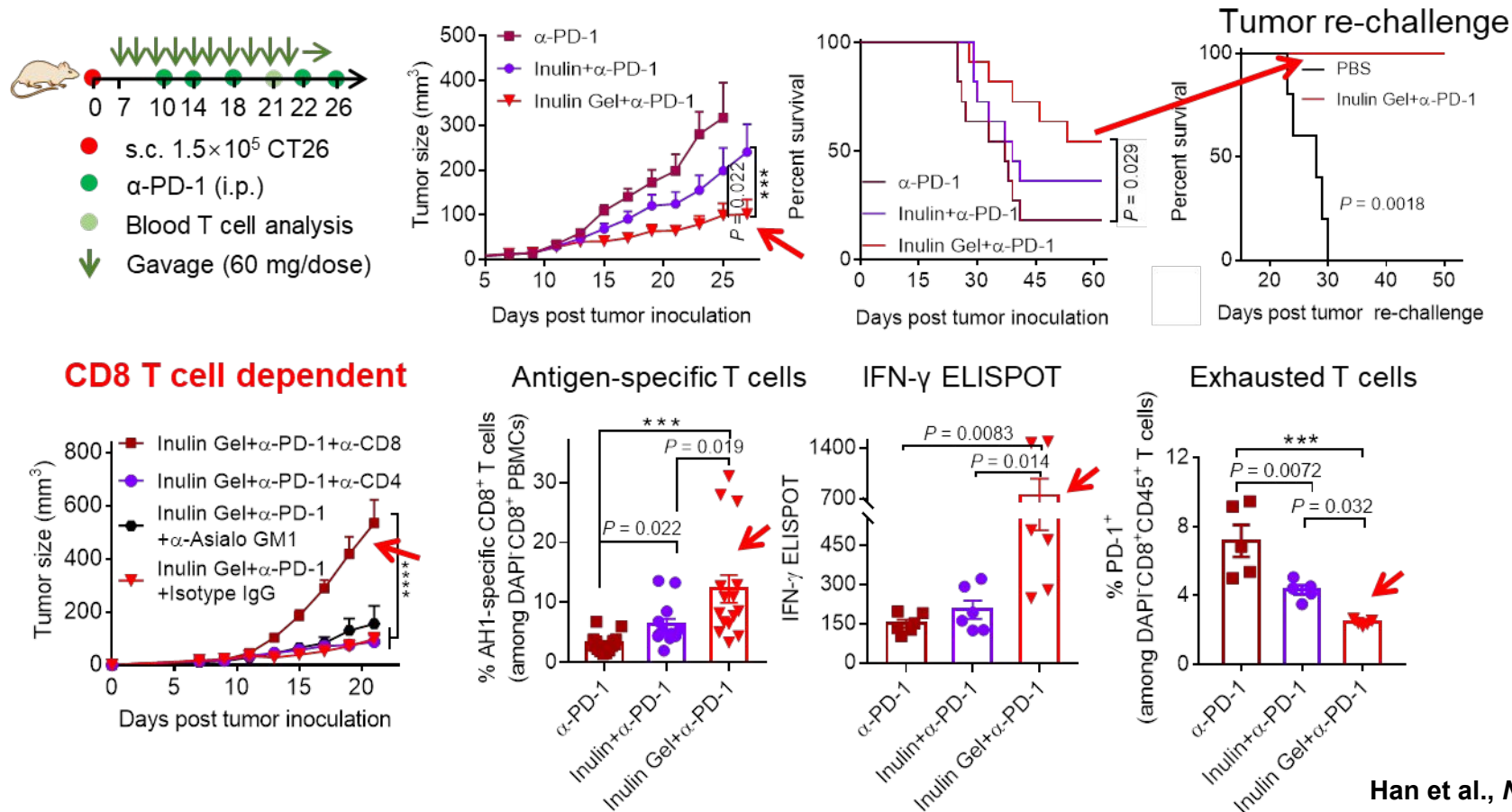


16S rRNA analysis



Han et al., *Nat. Biomed. Eng.*, 2021, 5, 1377-1388

Inulin gel improves therapeutic efficacy of α -PD-1, protects tumor-free mice against re-challenge



Han et al., *Nat. Biomed. Eng.*, 2021, 5, 1377-1388

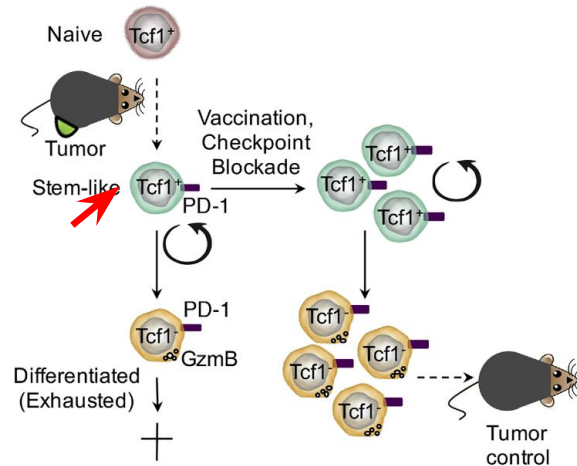


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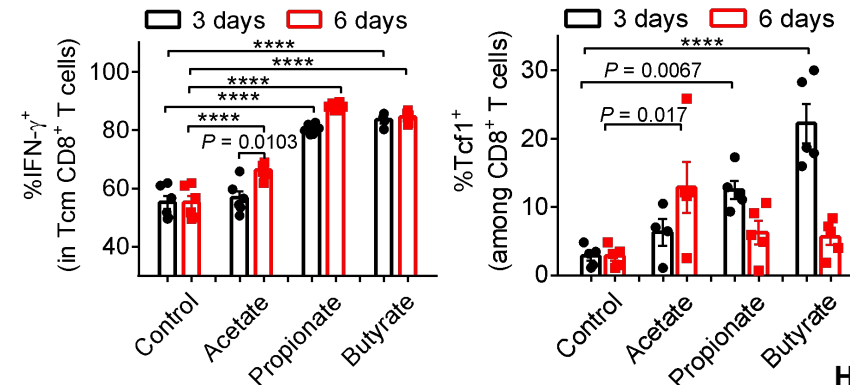
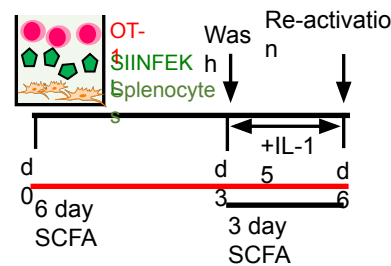
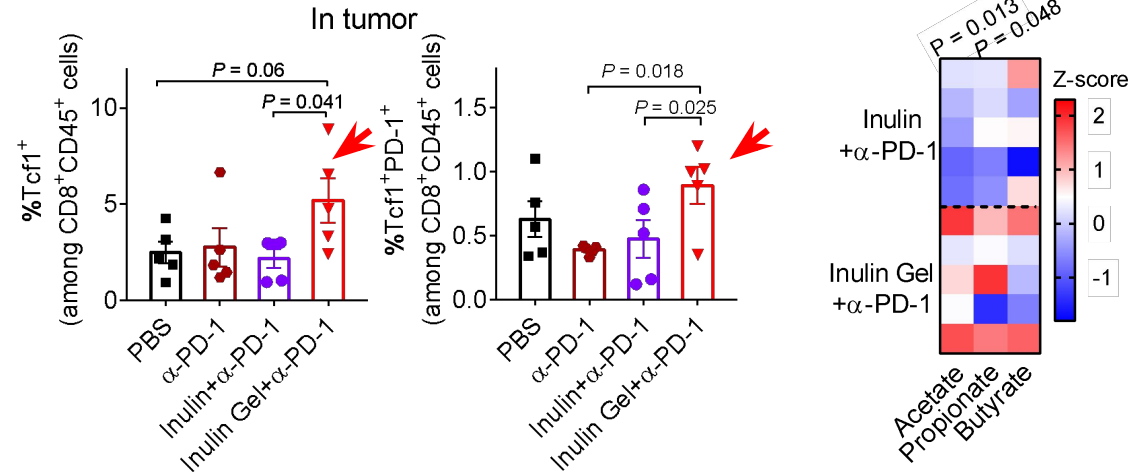
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Inulin gel plus α -PD-1 increase SCFAs and augment stem-like CD8⁺ T cells



Siddiqui et al., *Immunity* 2019, 50, 195–211



Han et al., *Nat. Biomed. Eng.*, 2021, 5, 1377-1388

Part II. Inulin gel/allergen formulation for oral immunotherapy



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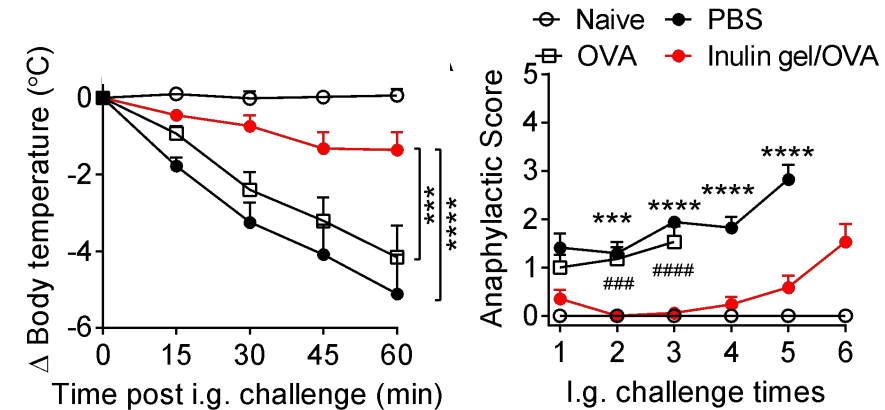
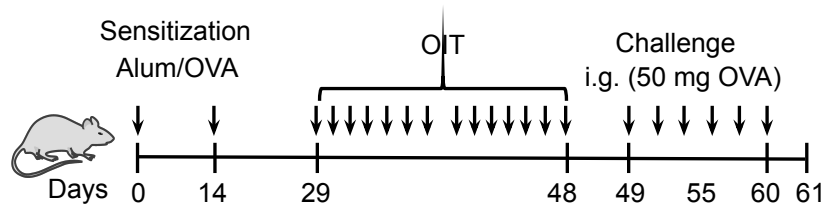
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OIT: oral immunotherapy

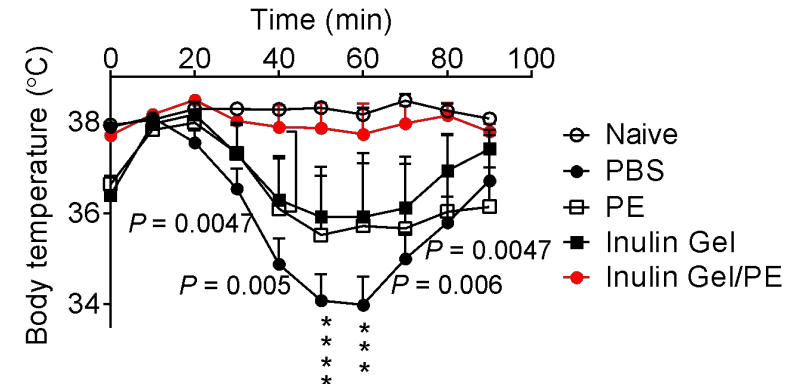
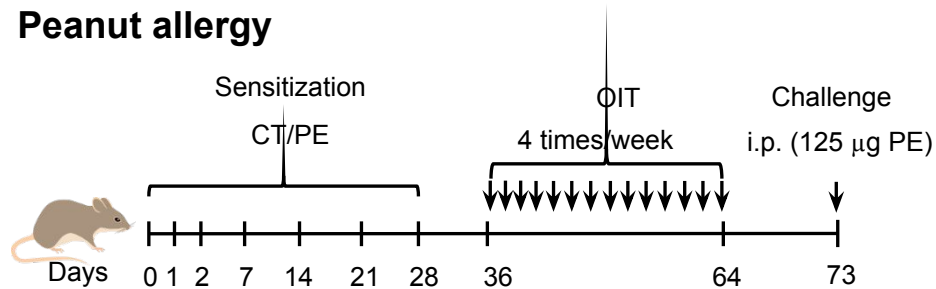
Unpublished data

Inulin gel/allergen formulation protects against food allergen challenge

Egg allergy



Peanut allergy



OIT: oral immunotherapy

Unpublished data



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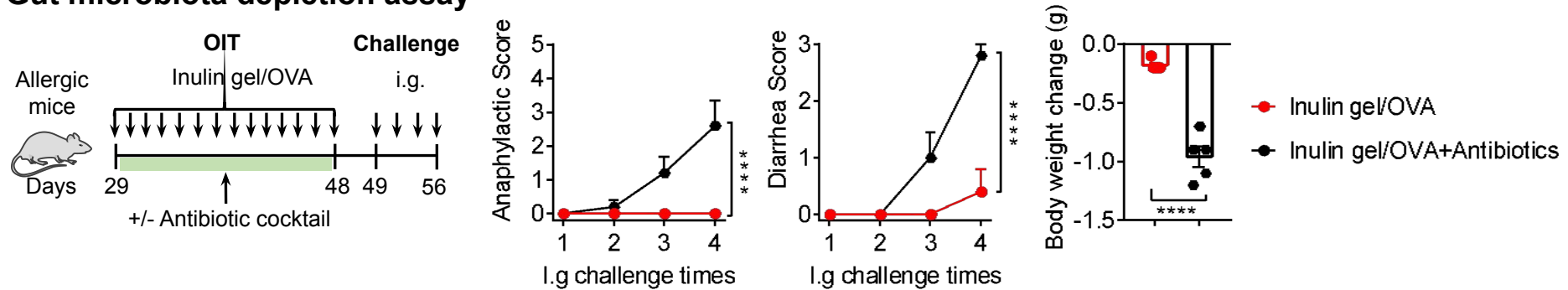
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OIT: oral immunotherapy

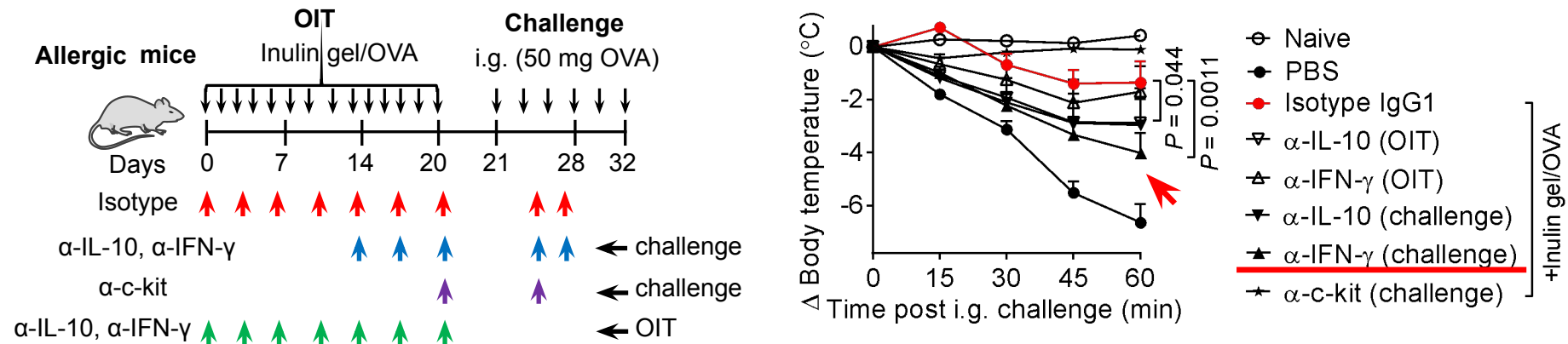
Unpublished data

The therapeutic efficacy of inulin gel/allergen OIT is dependent on gut microbiota and Th1 immune response

Gut microbiota depletion assay



Depletion assay *in vivo*



Unpublished data



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OIT: oral immunotherapy

Unpublished data

Summary

- Oral administration of inulin gel with higher viscosity effectively modulates the gut microbiota/metabolites, increases the abundances of “beneficial” microbes as well as the concentrations of SCFAs.
- Oral administration of inulin gel can synergize with ICB blockers and induce the stem-like CD8 T cells against tumor growth.
- Oral administration of inulin gel/allergen formulation establishes the tolerance in the small intestine and protects against food allergen challenges.



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OIT: oral immunotherapy

Unpublished data



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OIT: oral immunotherapy

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