KCRNC KIDNEY CANCER RESEARCH NETWORK OF CANADA
RRCRC RÉSEAU DE RECHERCHE SUR LE CANCER DU REIN DU CANADA

CRCHUM CENTRE DE RECHERCHE

Immune-Potentiating Impact of the Gut Microbiome on Kidney Cancer Immune Infiltrate: A Novel Predictor of Immune Checkpoint Inhibitors

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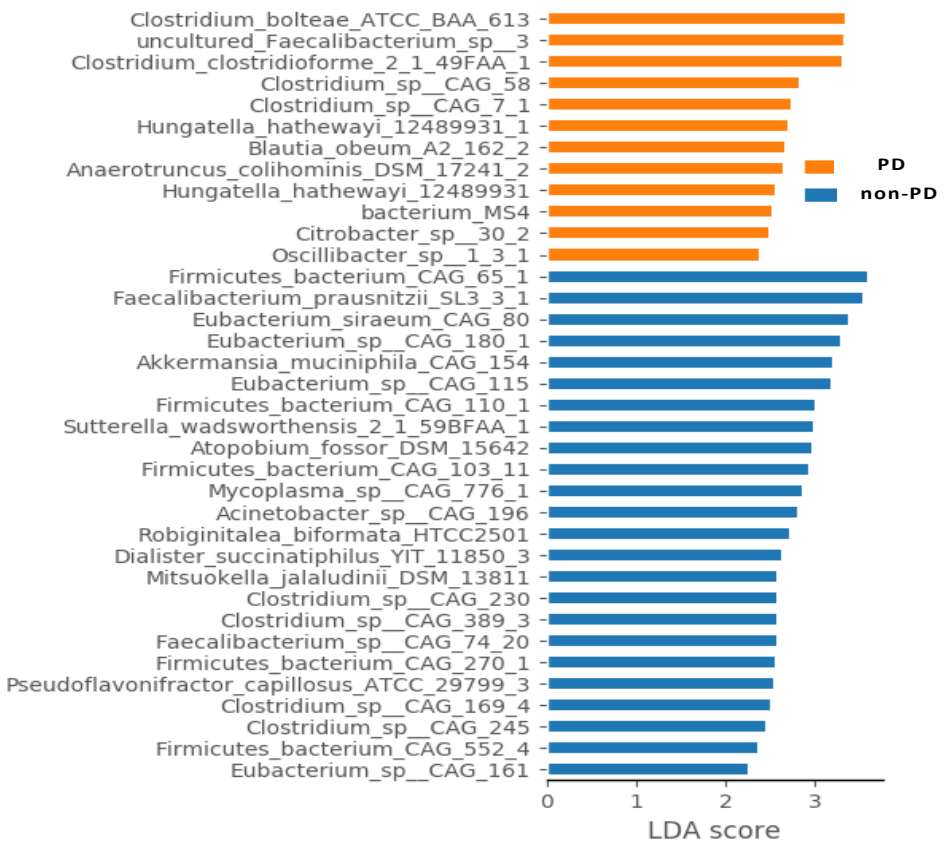
Gut microbiome to predict response and treat patients on IO



n=70 patients treated with relapse RCC on Nivolumab

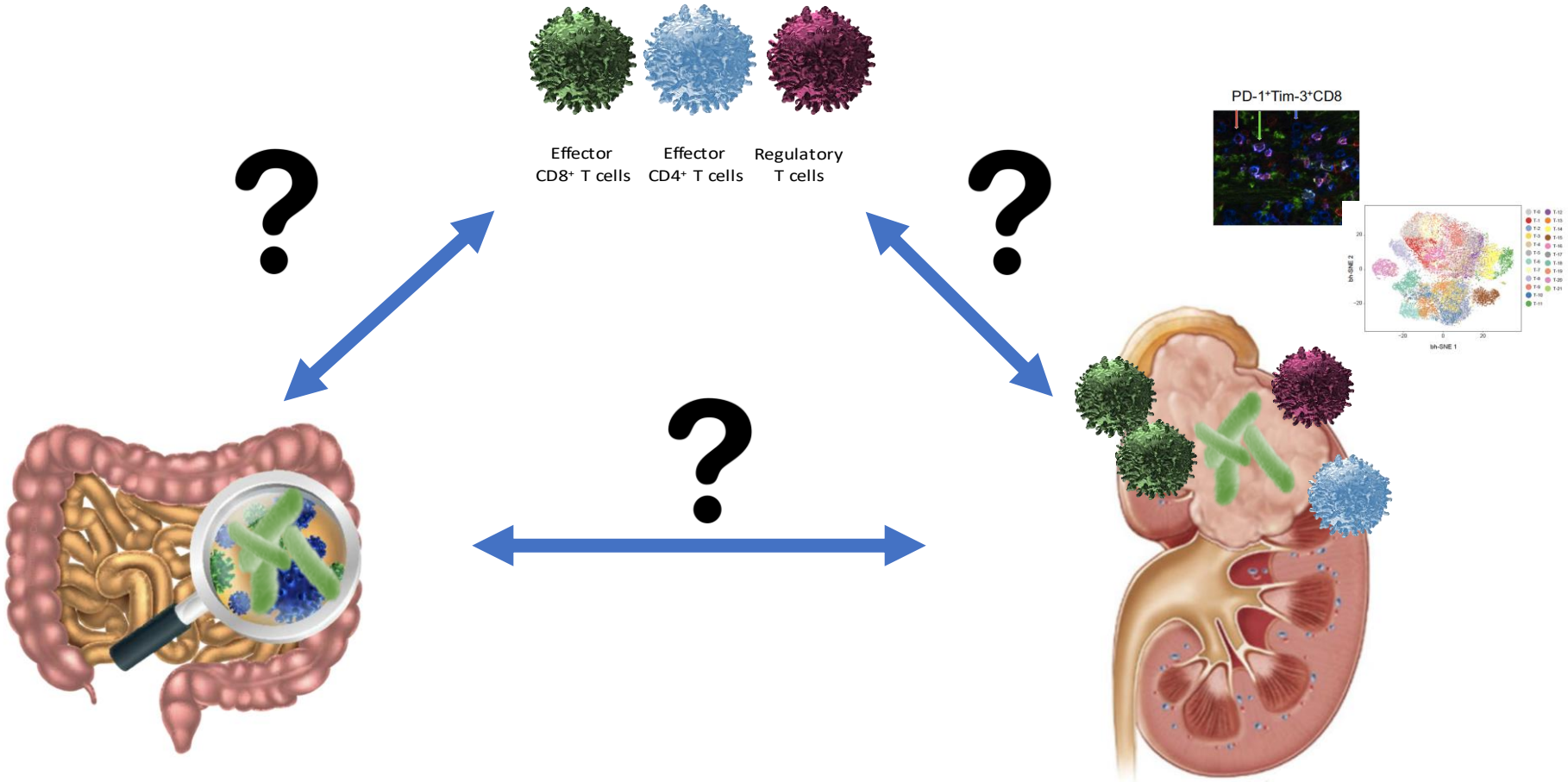
Derosa et al. ASCO 2018

AACR American Association for Cancer Research ANNUAL MEETING 2019 ATLANTA

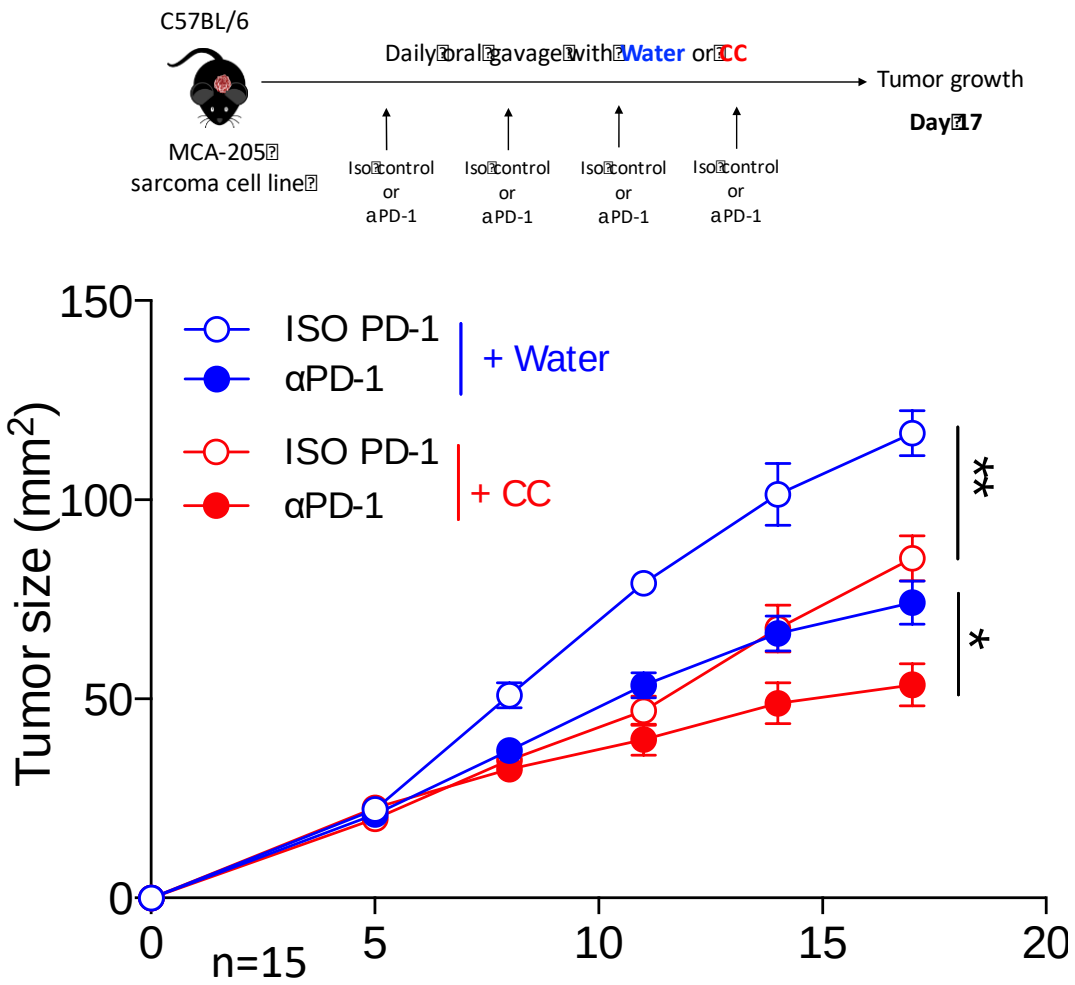
CT042 - Fecal microbiota transplantation (FMT) and re-induction of anti-PD-1 therapy in refractory metastatic melanoma patients - preliminary results from a phase I clinical trial (NCT03353402)

Conclusion: FMT in metastatic melanoma patients seemed to be safe and may alter recipient gut microbiota to resemble that of a responder donor. This alteration may result in intra-tumoral T-cell activity, which was translated to a clinical and radiological benefit in two recipients.

Aim of the project: Determine the impact of the gut microbiome on systemic immune response and intra-tumor bacteria



Modification of gut microbiome with polyphenol CC prebiotics improve anti-PD-1 response and transform PD-1 resistant tumor to immunosensivite



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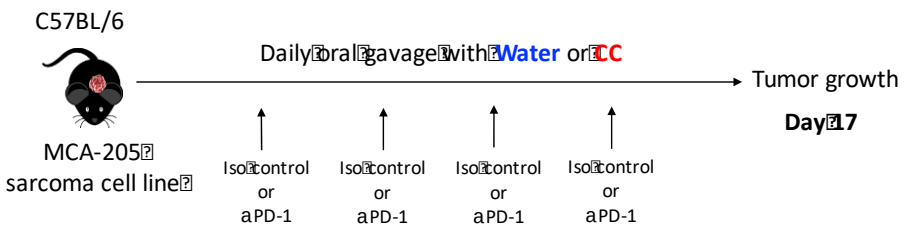
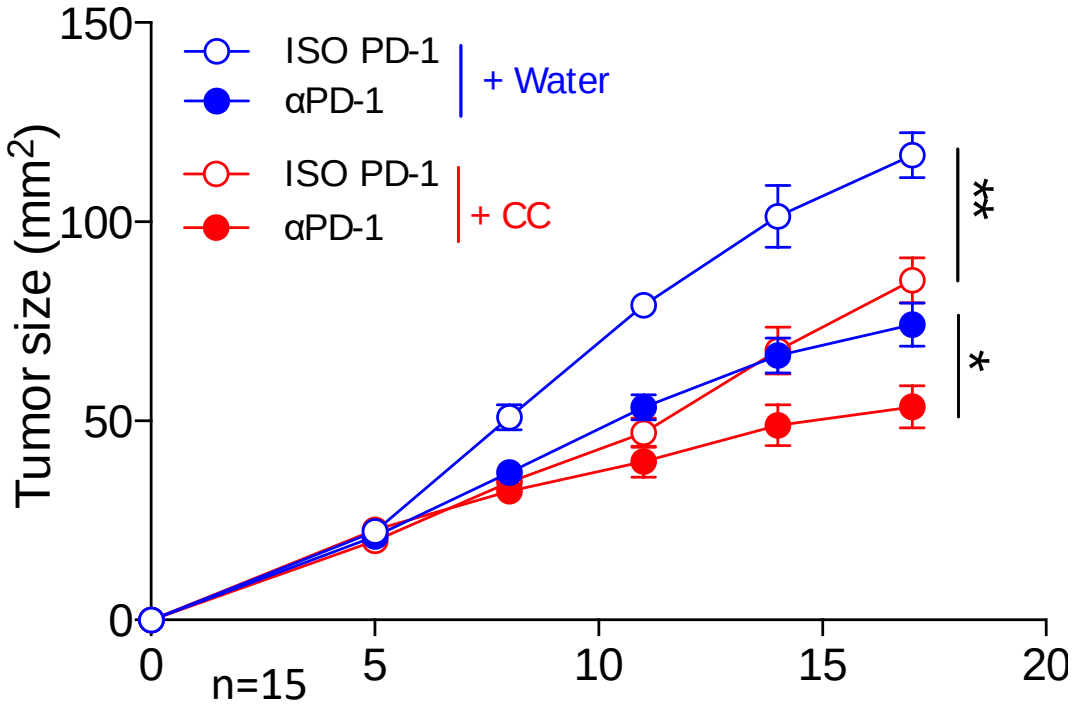
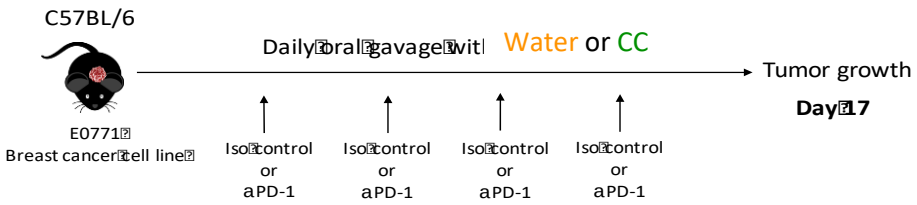
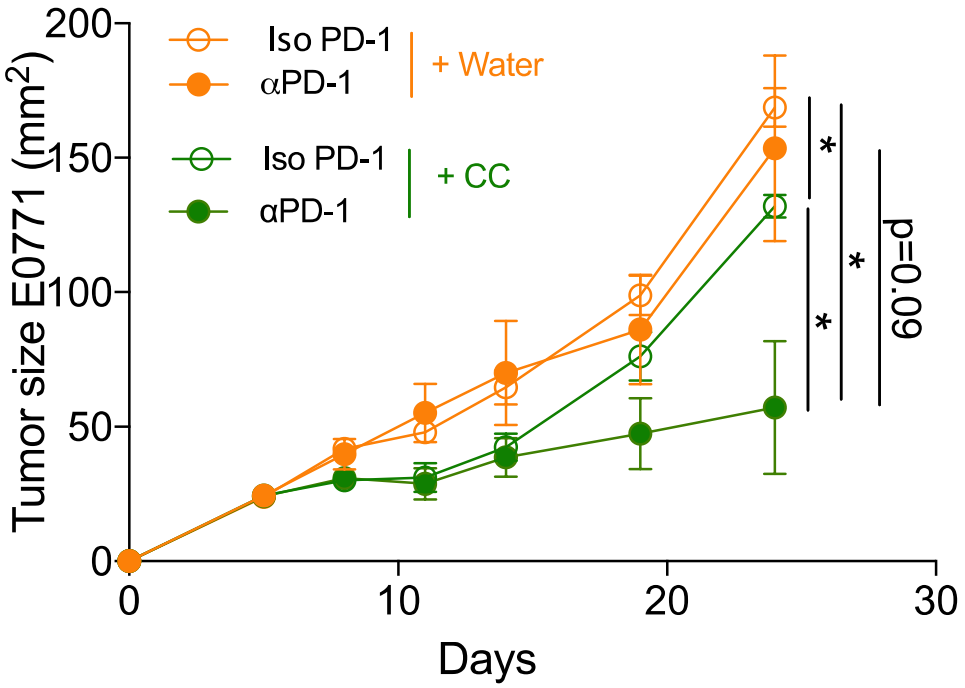




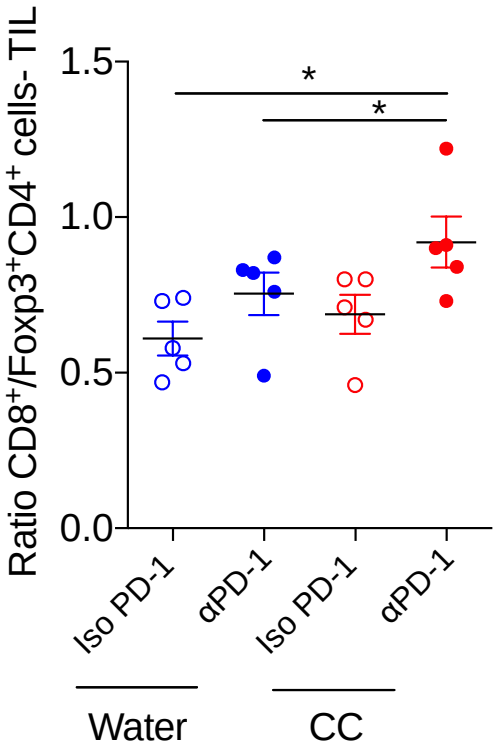


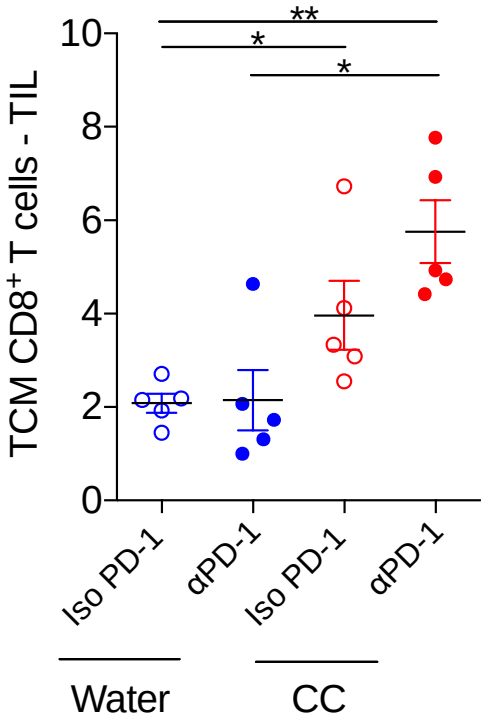


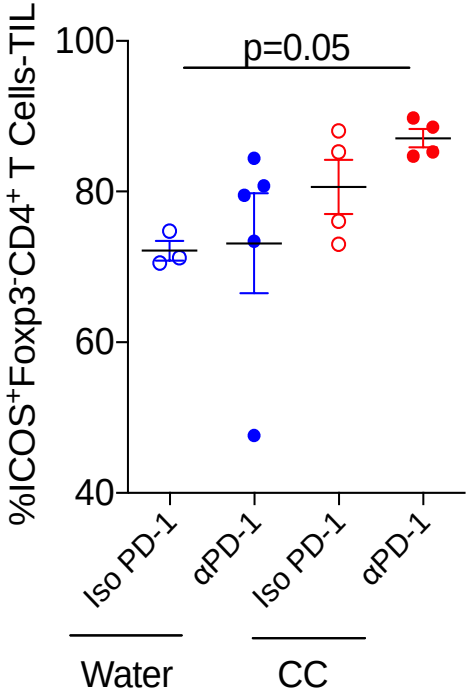
Immune surrogate markers of activity in the tumor microenvironment

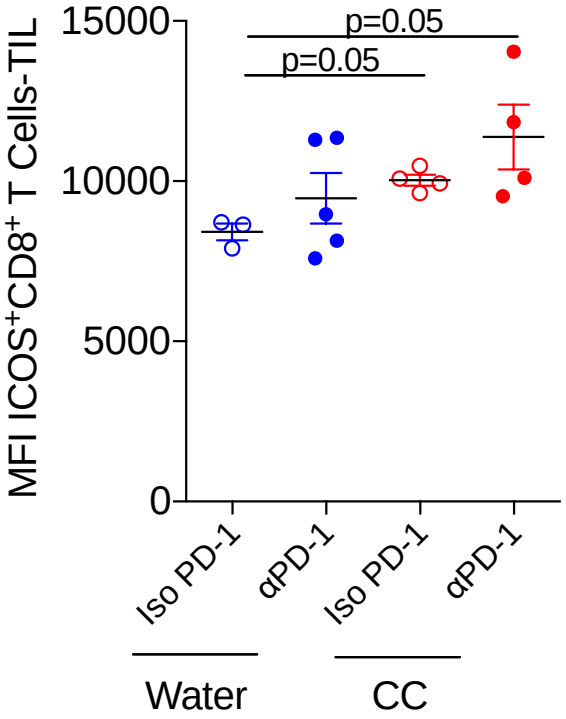
MCA-205

E0771









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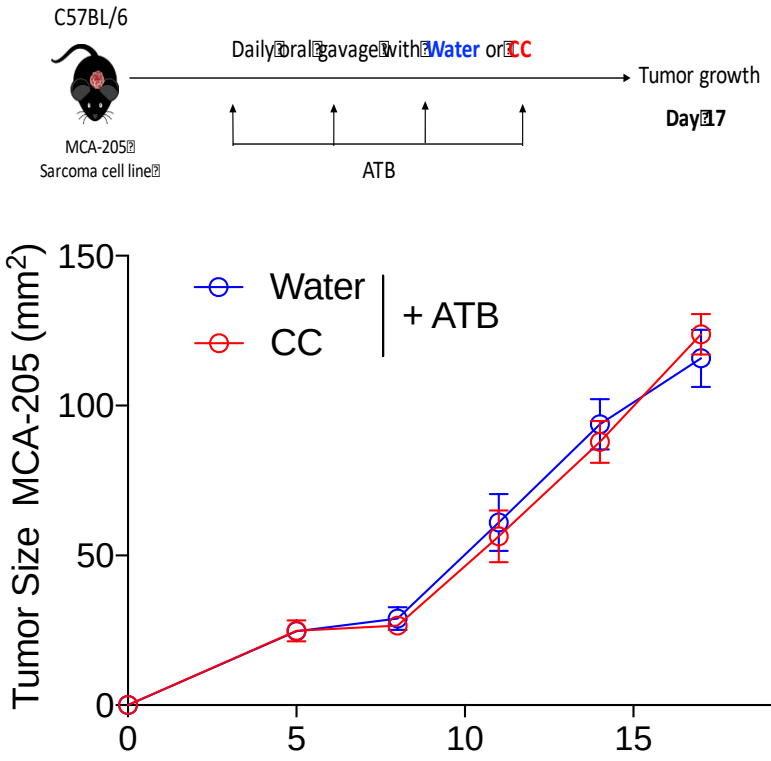
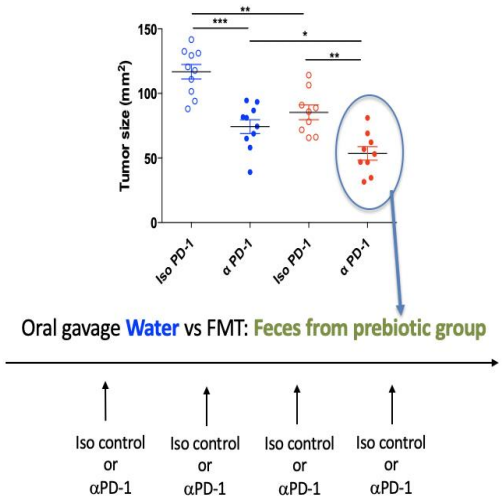
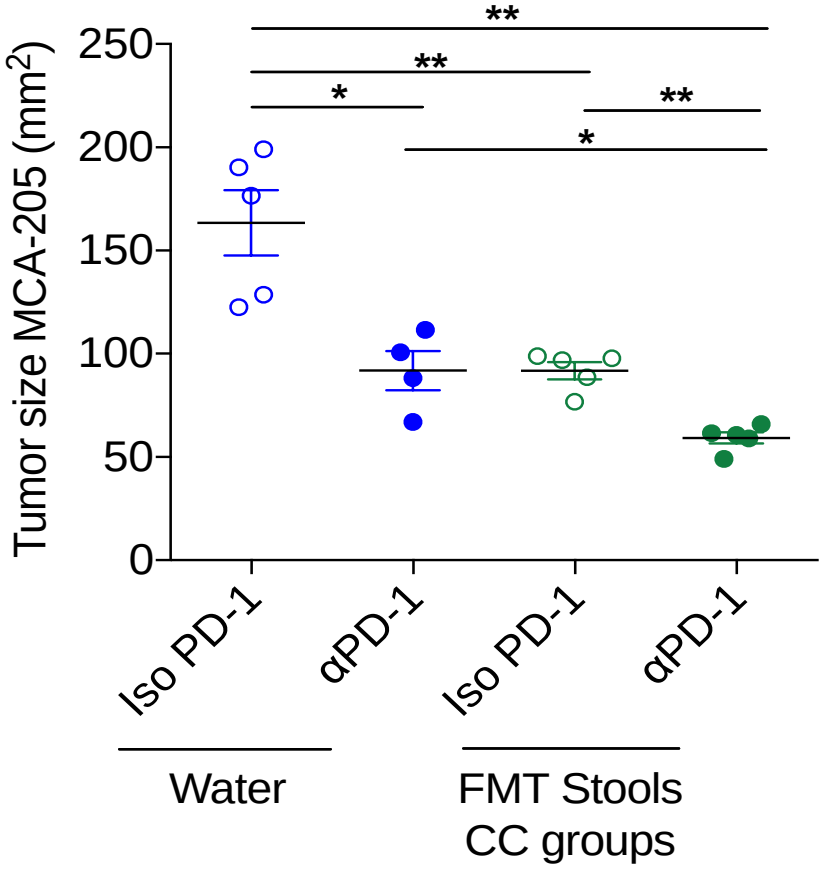
The anticancer activity of CC is microbiome dependent: Two lines of evidence







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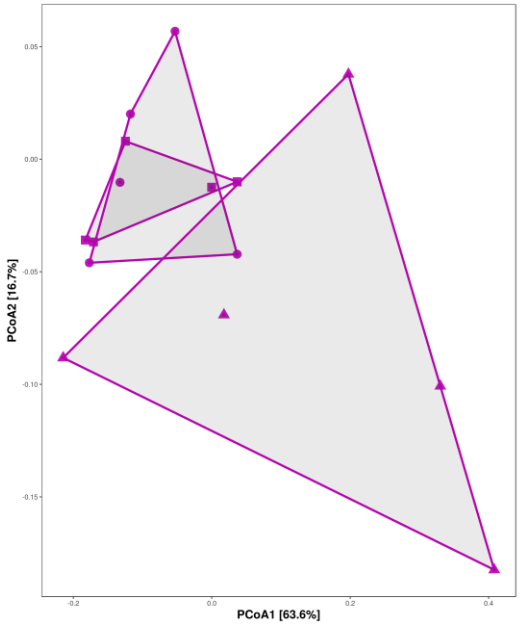
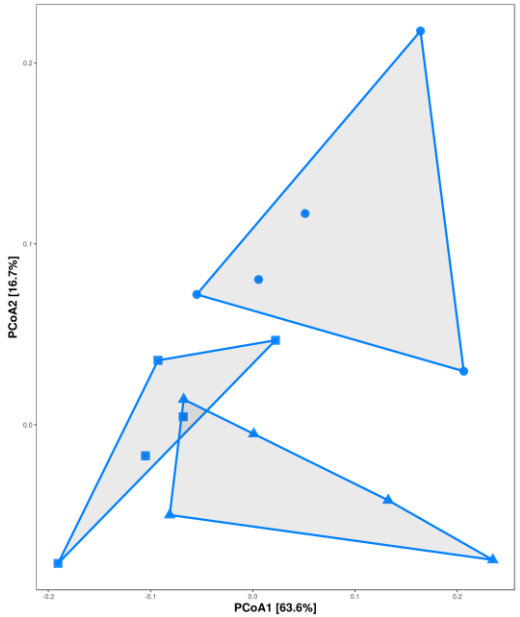
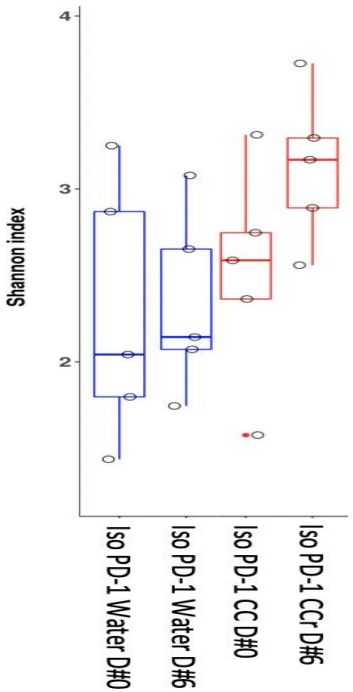
CC prebiotic shifts the microbiome composition and increase bacterial diversity

Water groups



CC groups





IsoPD-1 Water D#0
IsoPD-1 Water D#6
IsoPD-1 Water D#9

IsoPD-1 CC D#0
IsoPD-1 CC D#6 *
IsoPD-1 CC D#9

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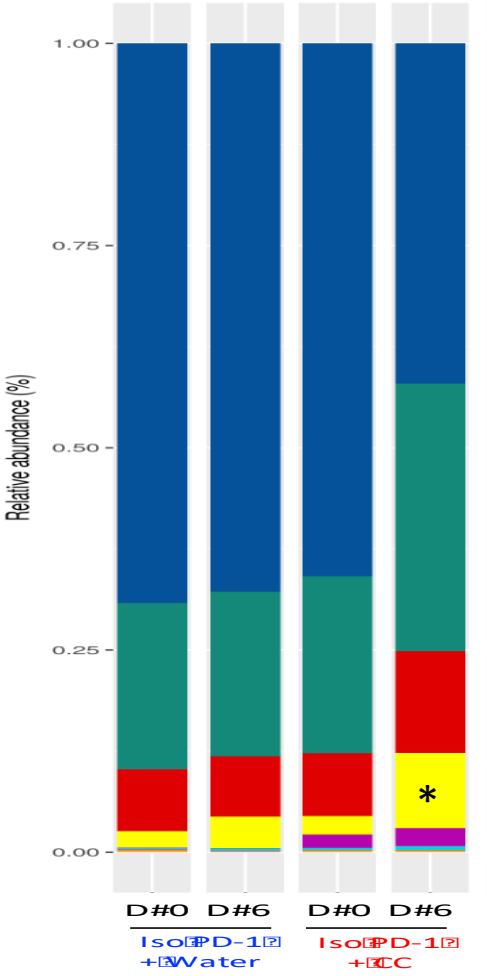
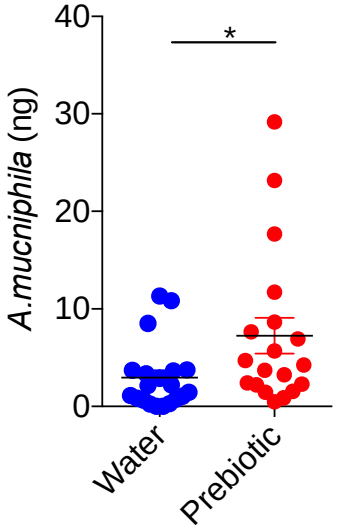
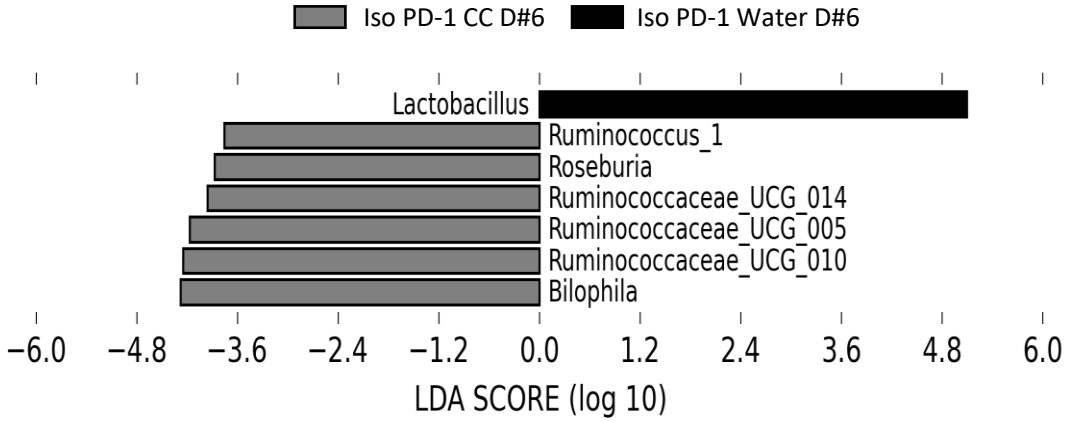
Post prebiotic both *Akkermansia muciniphila* (Routy Science 2018) and *Ruminococcaceae* (Gopalakrishnan Science 2018) are enriched







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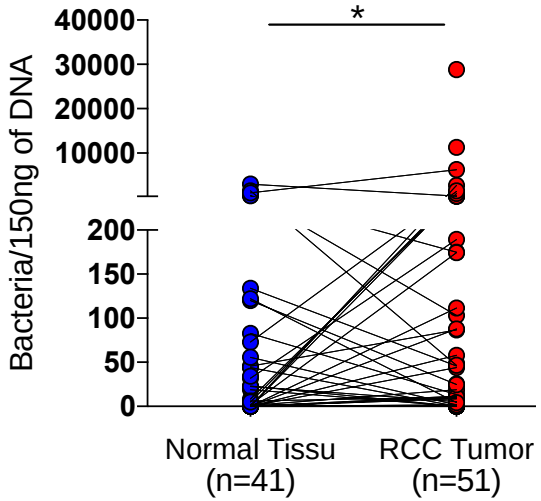
Influence of CC on intratumor bacteria
16s sequencing results

Human

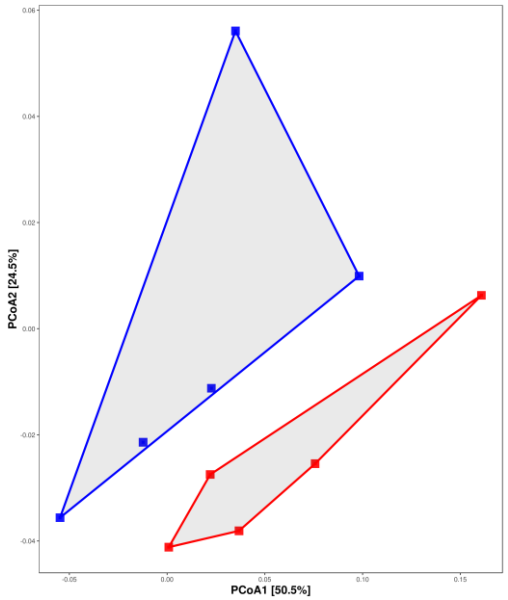
Intratumor bacteria – RCC are not sterile



	Normal Tissu (N=41)	Tumor RCC (N=51)
% Bacteria+	70,73 %	86,27 %
% Bacteria-	29,26 %	13,72 %

Mouse

Tumor



Tumor IsoPD-1 Water
Tumor IsoPD-1 CC
**

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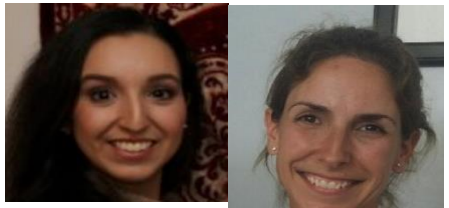
Conclusions

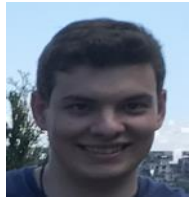
1- Identification a polyphenol prebioctic capable of positively changing the gut microbiome composition, boosting diversity, Akkermansia muciniphila and ruminoccocus. This changes translated in stronger immune response (Higher CD8-ICOS, higher frequency of TCM CD8) and clinical efficacy.

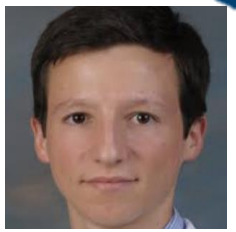
2- Tumors are not sterile and RCC tumor are colonized with more bacteria than adjacent tissue.

3- More funding and another CKCJ grant would be needed to further link the possibility that the gut microbiome dictates anti-cancer response an intra-tumor bacteria in RCC.

Acknowledgements





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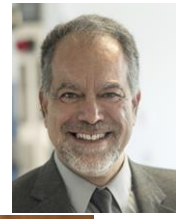


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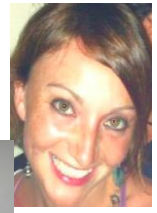

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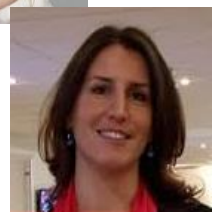

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