EVELO BIOSCIENCES

MONOCLONAL MICROBIALS AND CANCER THERAPY

Cancer Drug Development Forum
Munich, 16 February 2019

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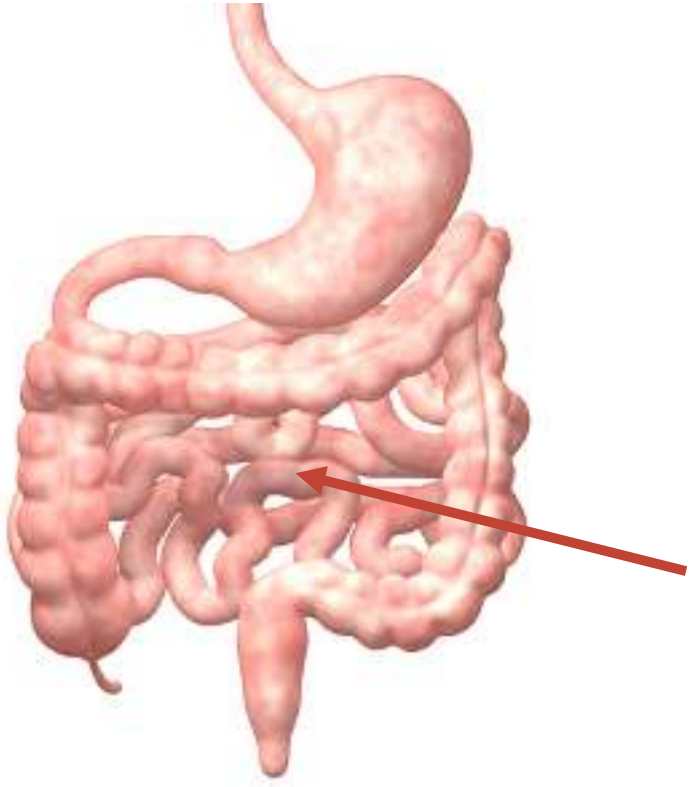
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including our development plans, the promise and potential impact of any of our monoclonal microbials or clinical trial data, timing of and plans to initiate clinical studies of EDP1503, EDP1066 and EDP1815, the timing and results of any clinical studies, and the sufficiency of cash to fund operations.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our limited operating history; our unproven approach to therapeutic intervention; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in regulatory approval; our reliance on third parties and collaborators to expand our microbial library, conduct our clinical trials, manufacture our product candidates, and develop and commercialize our product candidates, if approved; our lack of experience in manufacturing, selling, marketing, and distributing our product candidates; failure to compete successfully against other drug companies; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; our patents being found invalid or unenforceable; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; our management and principal stockholders have the ability to control or significantly influence our business; a significant portion of our total outstanding shares are eligible to be sold into the market in the near future; costs and resources of operating as a public company; unfavorable or no analyst research or reports; and securities class action litigation against us.

These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

The Gut has Distinct Functional Regions and Microbial Content



Large Intestine

- ~99.99% of gut microbiome biomass, mainly luminal
- 10-20% of gut surface area
- Complex, diverse, variable by stool profiling

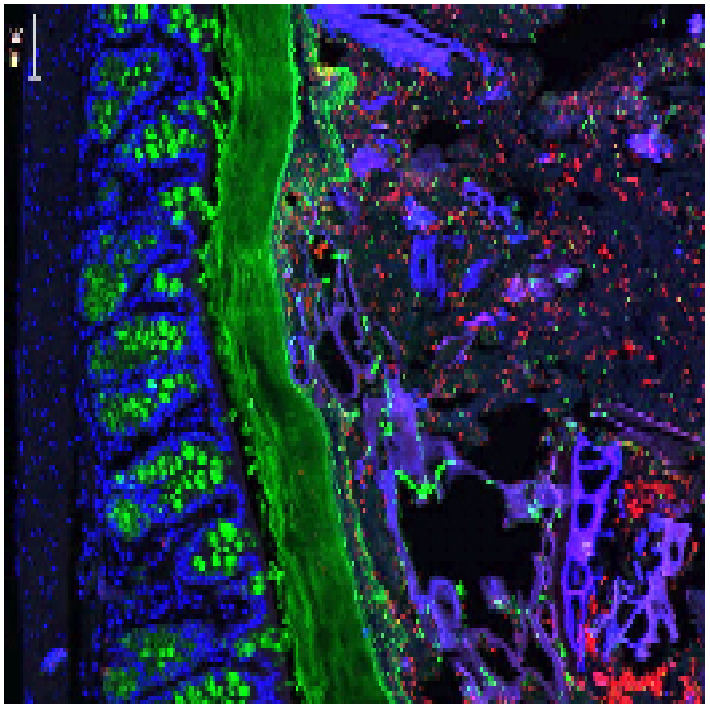
Remodeling with consortia (mixtures) of bacteria

Small Intestine

- ~0.01% of gut microbiome biomass, mucosal
- 80-90% of gut surface area
- Different microbial composition, intimately associated with host gut
- Epithelium includes a wide range of specialized cells
  - Immune, endocrine, neural

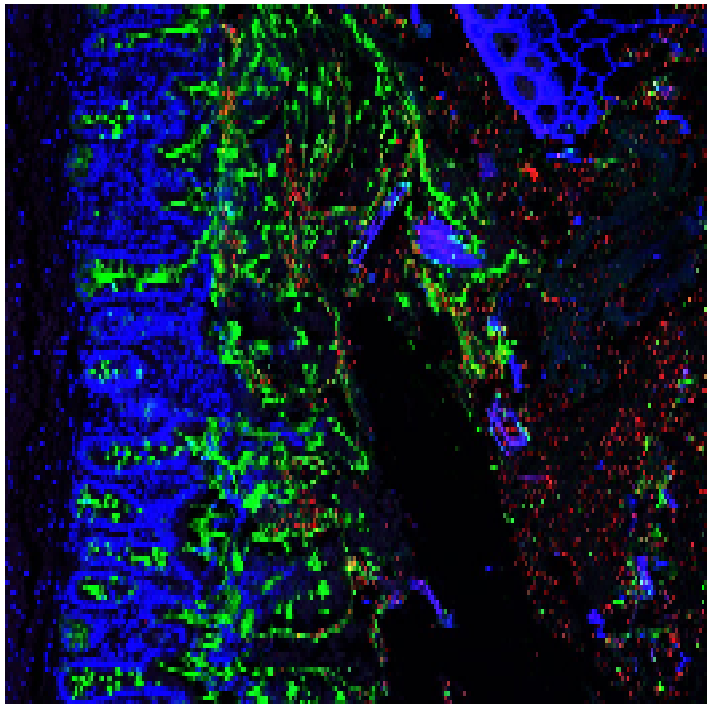
Monoclonal microbials can act directly on these host cells coordinating a wide range of systemic physiology

Cells in the Small Intestine are Accessible to Microbial Drugs



Large Intestine

Thick mucus (green)
limiting microbial contact



Small Intestine

Thin, fragmented mucus
allowing microbial contact

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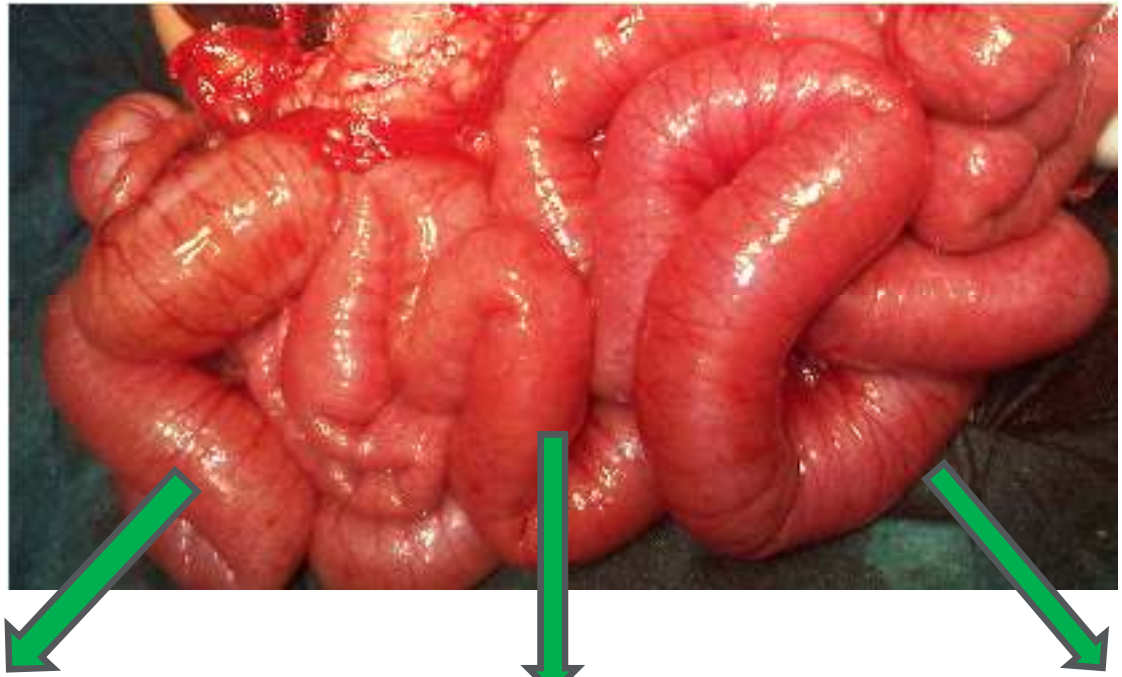
Evolutionarily Validated Biology

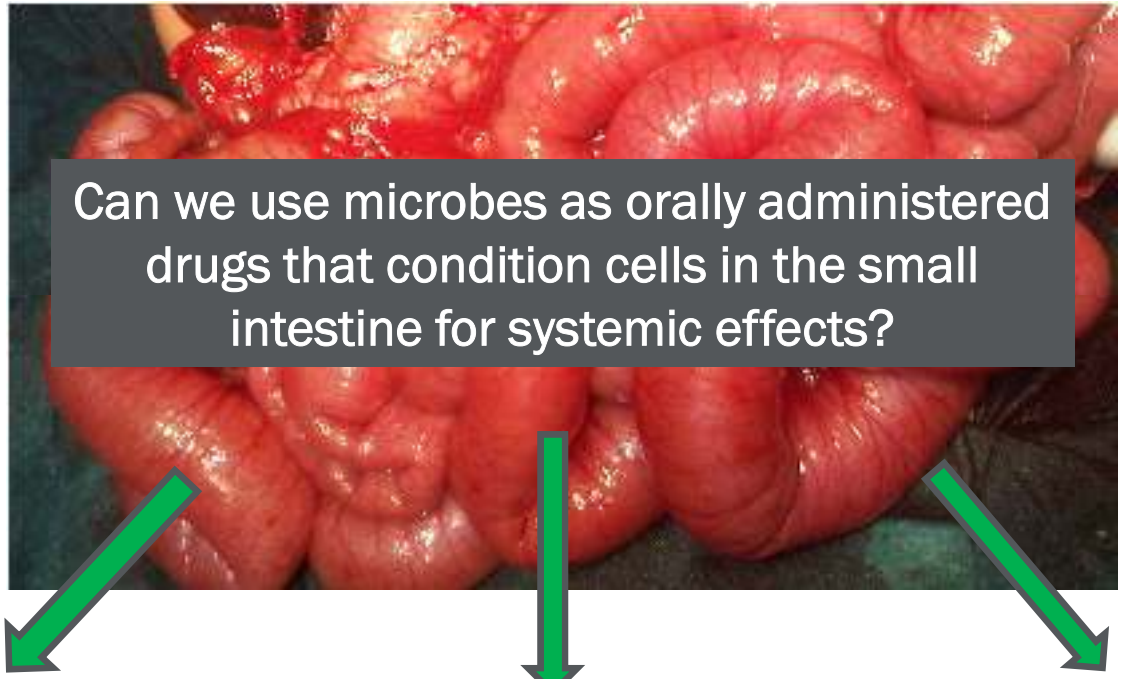
The gut-body network may affect the underlying biology of many diseases



Immunity Metabolism/CV Neurology

Evolutionarily Validated Biology

The gut-body network may affect the underlying biology of many diseases



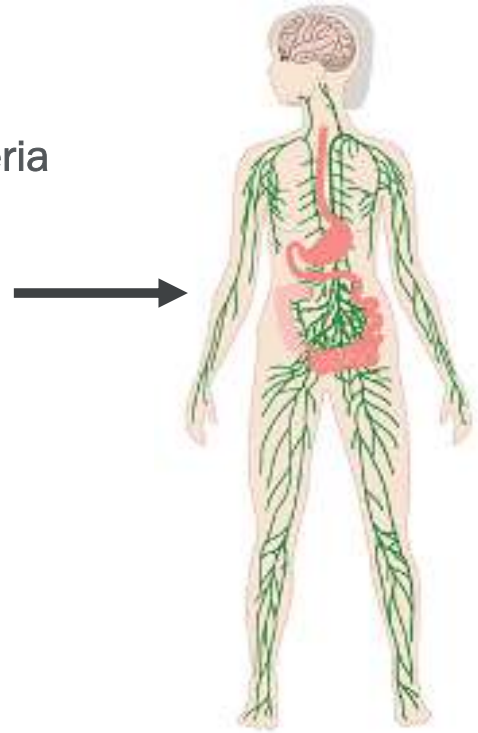
Immunity

Metabolism/CV

Neurology

Monoclonal Microbials: Oral Single Microbial Strains that Act on Immune Cells in the Small Intestine for Systemic Effects

- Single clonal strains of commensal bacteria
- Dose-dependent effects
- Choice of strain matters
- GMP manufacturing to clinical quality



- Target immune cells in the SI (rather than the microbiome)
- Distribution is gut-restricted
- Pharmacology is systemic
- Do not colonize and many are effective replication-deficient

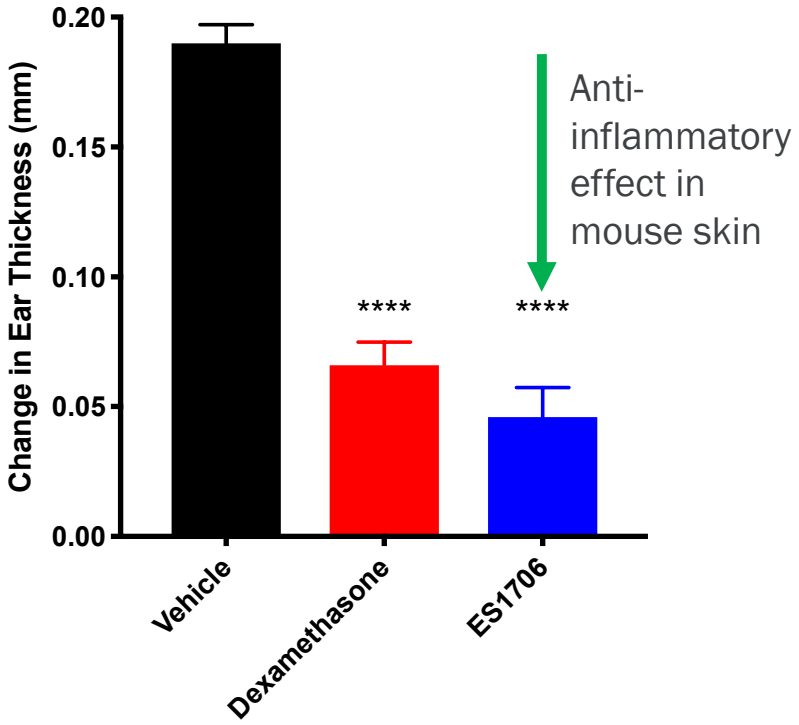
Evelo Platform for Selection and Development of Product Candidates

SOURCE	SELECT	DEVELOP	
MICROBIAL LIBRARY	ASSAYS & BIOLOGY	PROCESS DEVELOPMENT & MANUFACTURING	FORMULATION
Strains collection from various regions of the gut	Match human *in vitro* and mouse *in vivo* assays	Fermentation and lyophilization	Formulate for optimized pharmacology

In vitro Human Assays

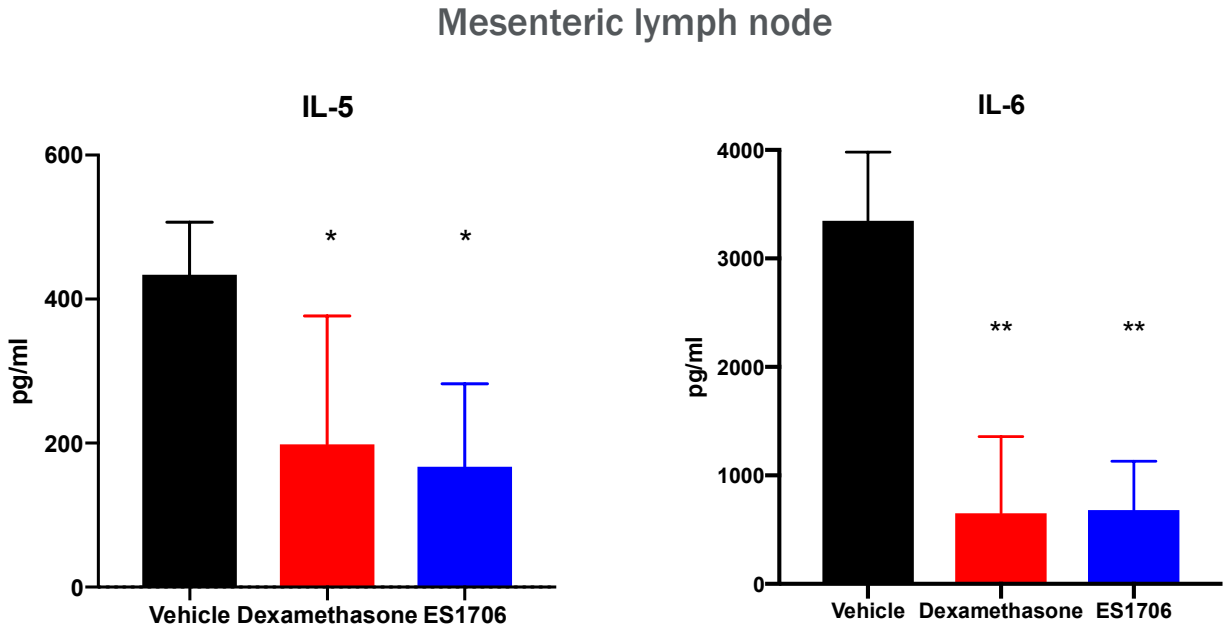
Animal Models

Anti-Inflammatory Efficacy of ES1706 is Profound

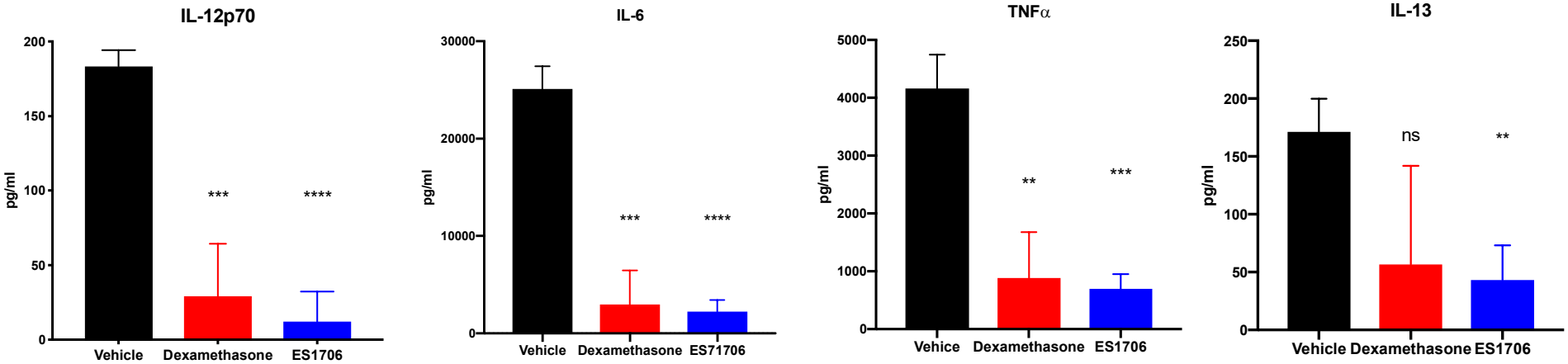


- ES1706 is a single strain of bacteria, given orally
- The drugs acts in the small intestine
- The anti-inflammatory effect is systemic

There are Effects in Small Intestinal Lymph Nodes…



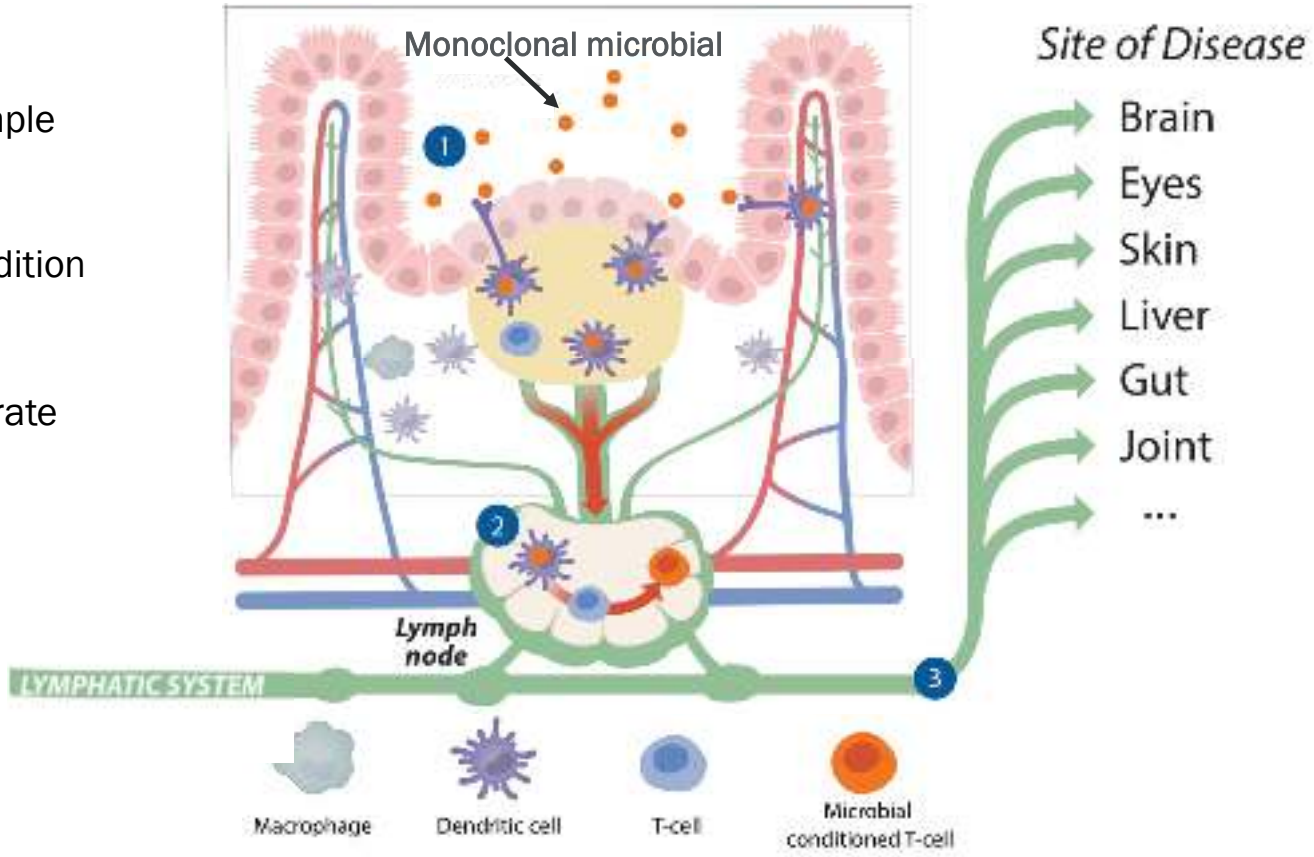
...that Track to the Site of Inflammation – The Gut-Body Network



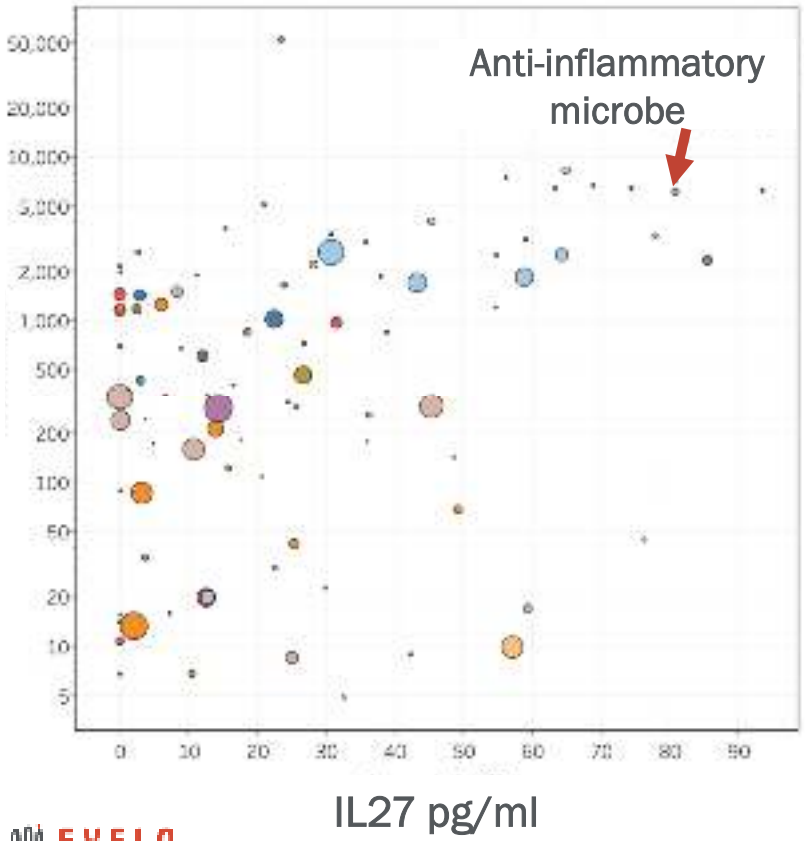
This is an extraordinary coordinated effect on multiple clinically validated pathways of inflammation by a drug acting in the small intestine which does not have to get to the site of disease

Monoclonal Microbials Condition Immune Cells in the Small Intestine

1. Sample
2. Condition
3. Migrate



Human Cellular Assays Mirror Immune Effects in Mouse Models



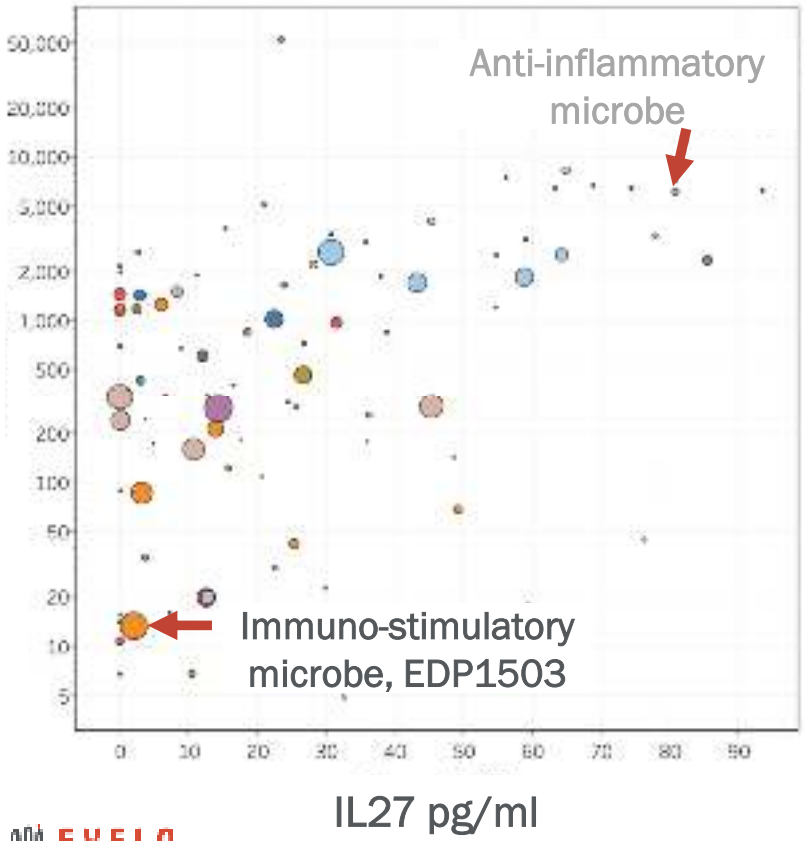
In vitro screen of ≈200 commensal strains for effects on human macrophages

Anti-inflammatory (EDP1066) in upper right

- High IL10
- High IL27
- Low CXCL10 (size of circle)

Color-coding is by genus

Immunological Effects are Reversed for Cancer – EDP1503



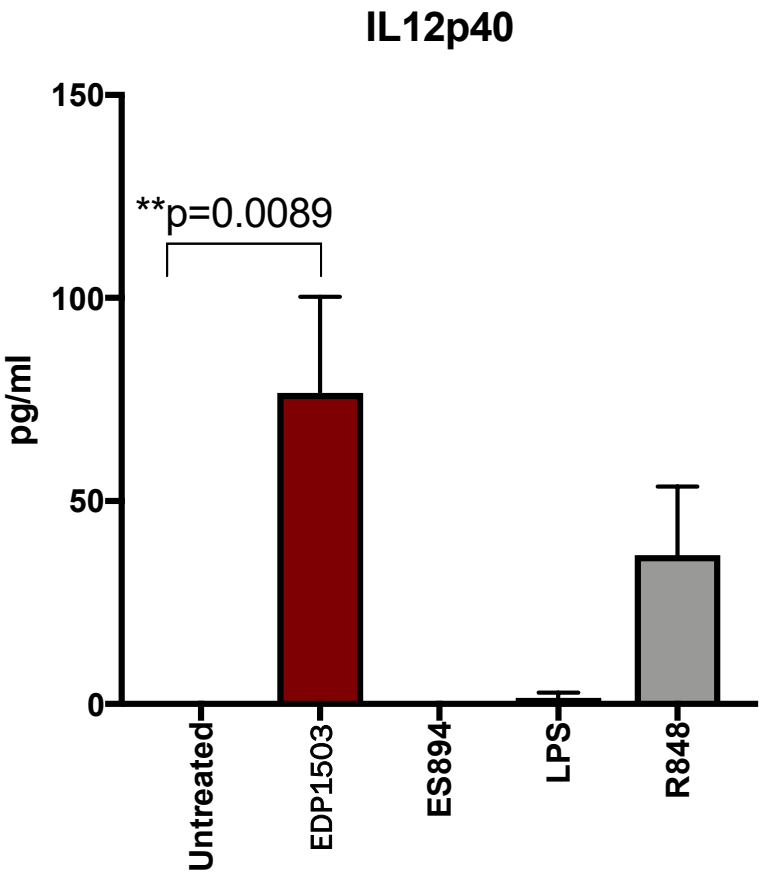
In vitro screen of ≈200 commensal strains for effects on human macrophages

Immuno-stimulator (EDP1503) in lower left

- Low IL10
- Low IL27
- High CXCL10 (size of circle)

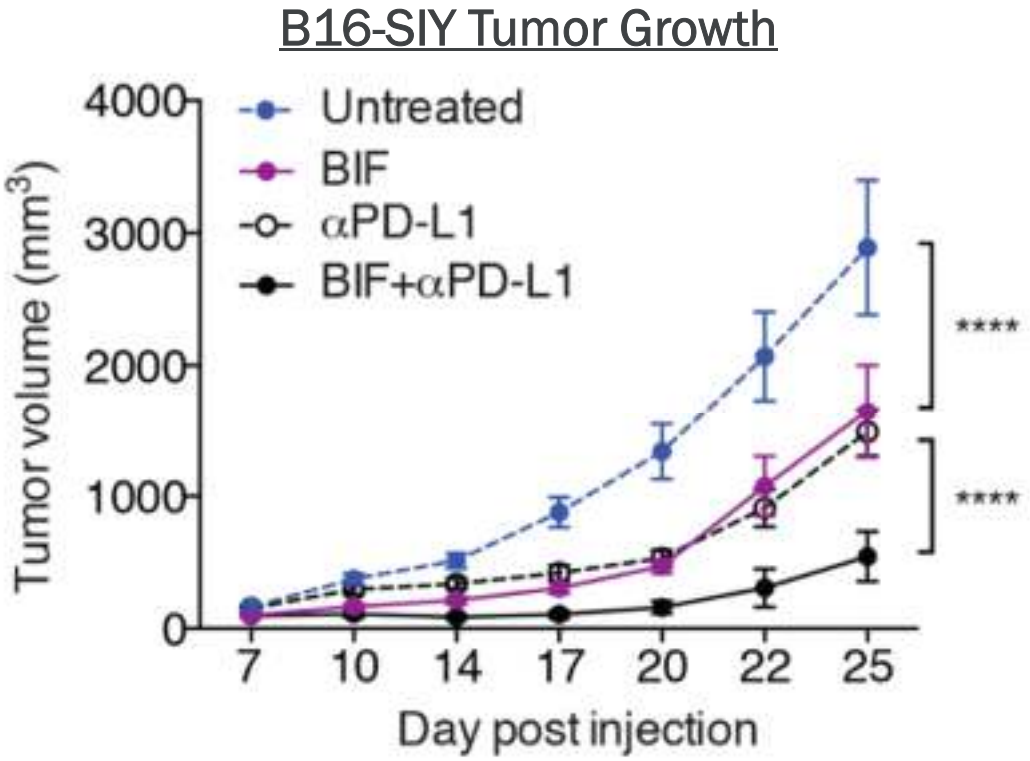
Color-coding is by genus

EDP1503 Stimulates Secretion of IL12 in Human Dendritic Cells



- 6 human donors. 18 hr incubation. MoI 1:1
- ES894 is an anti-inflammatory control microbe
- R848 (resiquimod), TLR7/8 agonist

Oral Bifidobacterium Promotes Anti-Tumor Immunity and Facilitates Anti-PD-L1 Efficacy

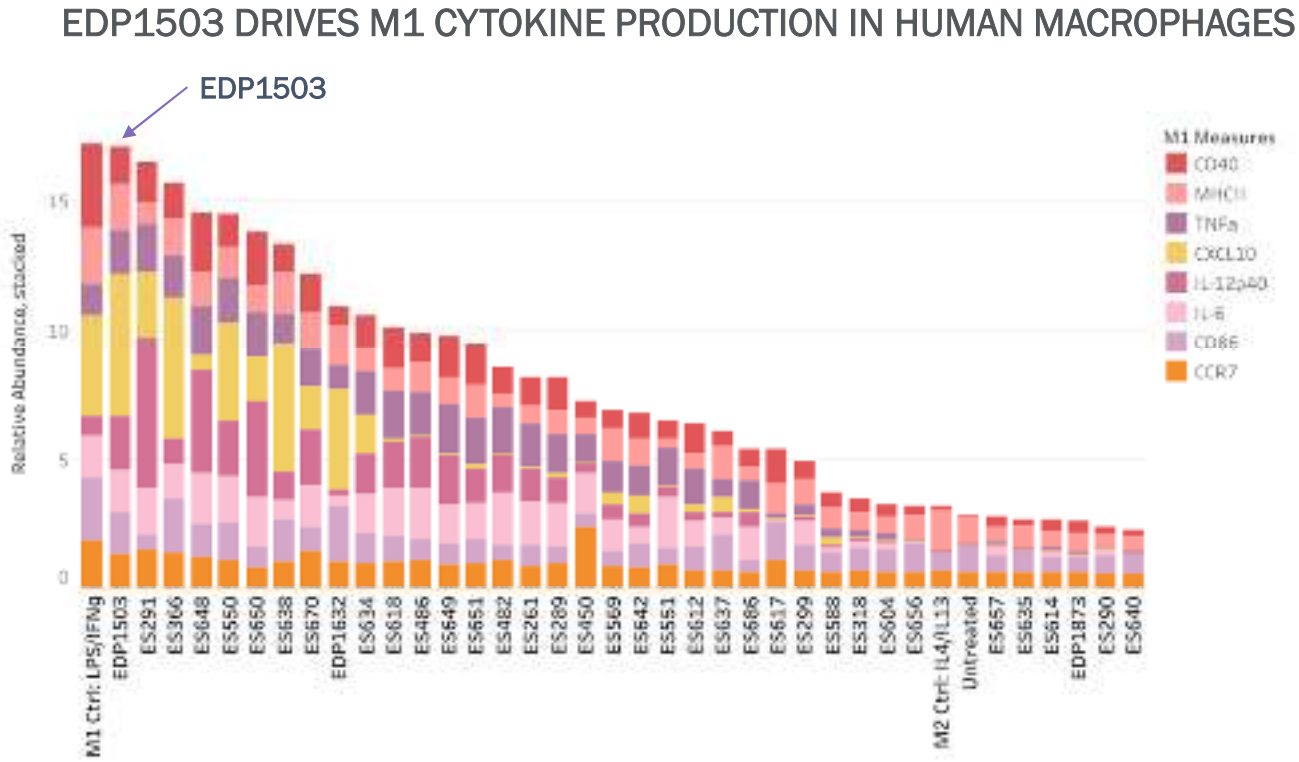


Remarkable therapeutic effect of oral commensal therapy from Gajewski lab

Basis of a broad approach to screening commensal bacteria for immuno-oncology

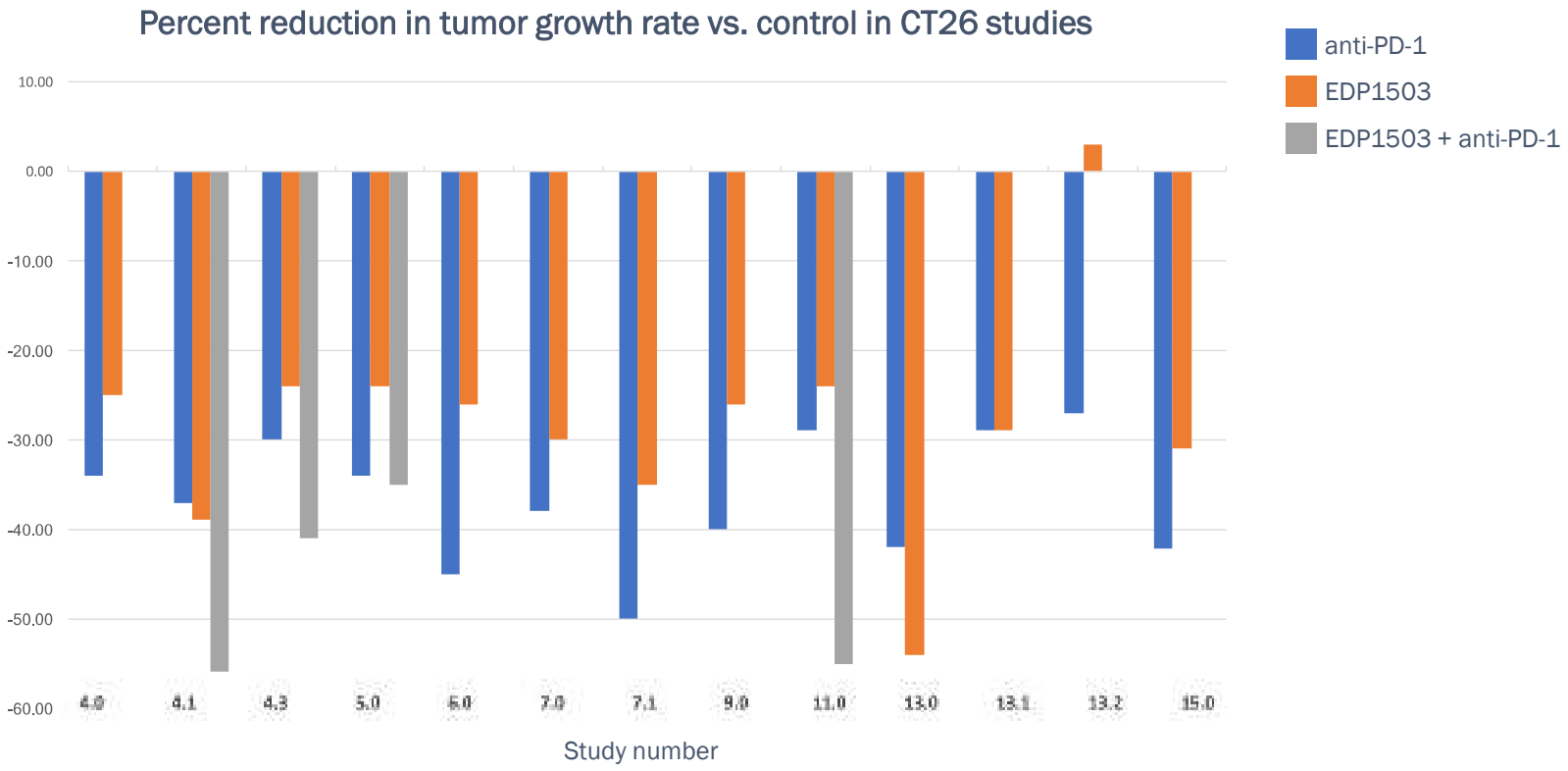
Sivan et al. 10.1126/science.aac4255 (2015)

Human Macrophage Screen of Bifibacterium Strains

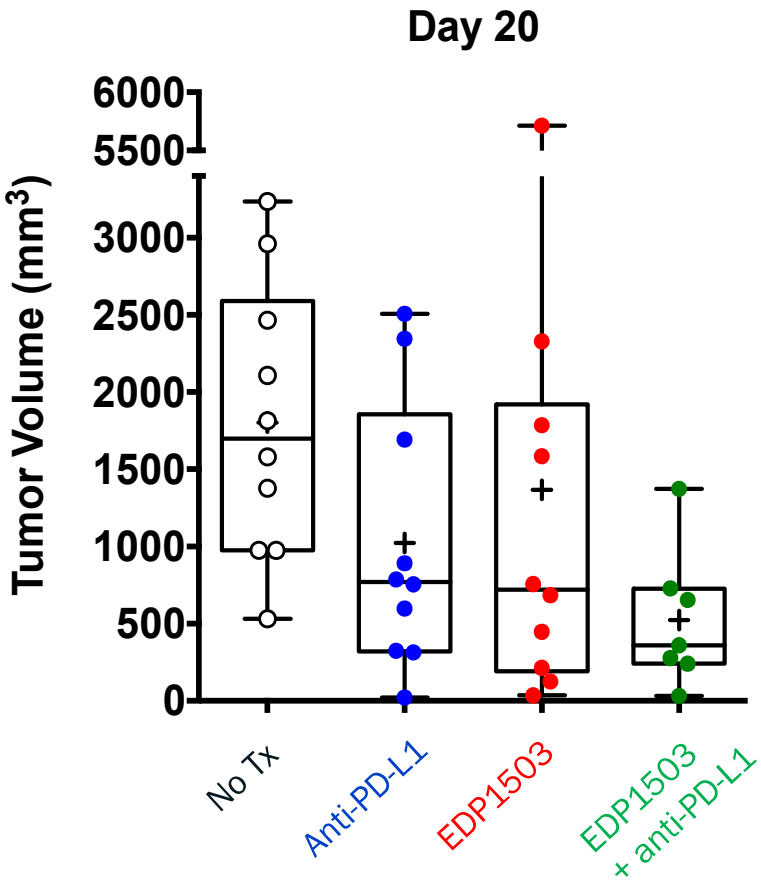


In parallel, these strains were screened *in vivo* in CT26 tumor model

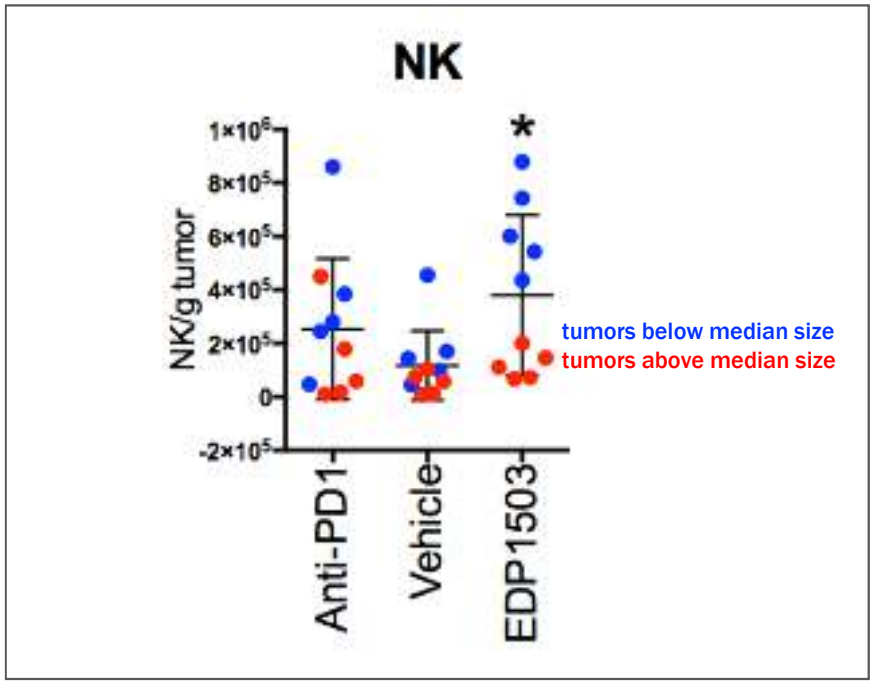
EDP1503 Shows Consistent Efficacy Compared to Anti-pd-1 In Multiple CT26 Studies and Combinatorial Effect

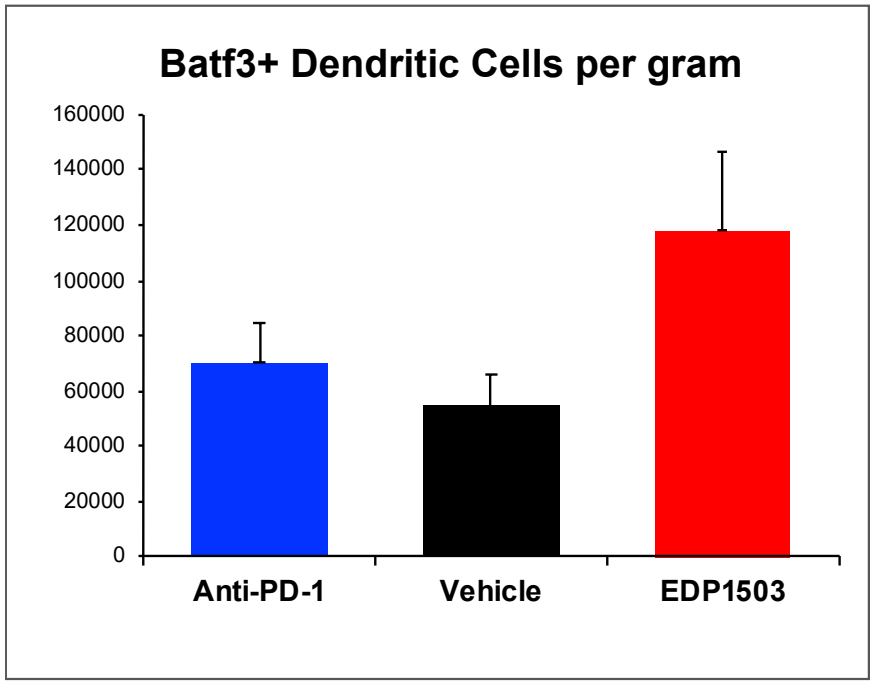


Orally Delivered EDP1503 in B16.F10 Tumor Model

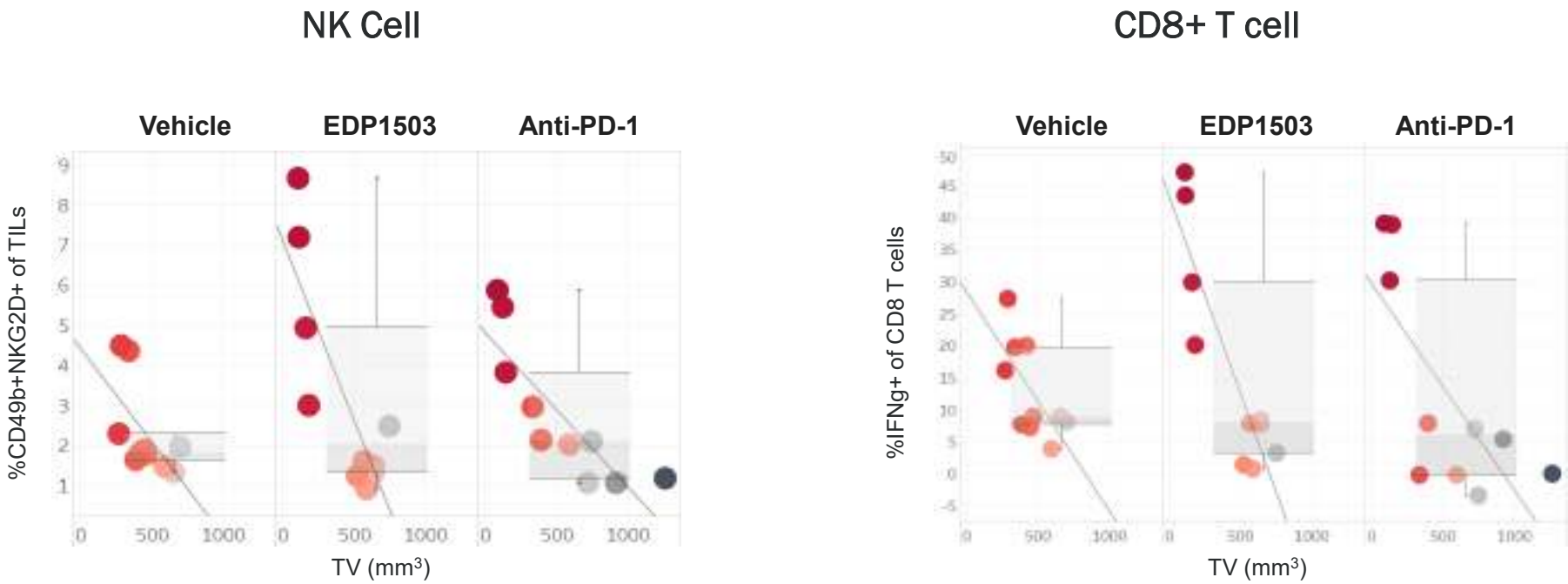


EDP1503 Increases NK and Dendritic Cells in Mouse CT26 Tumors



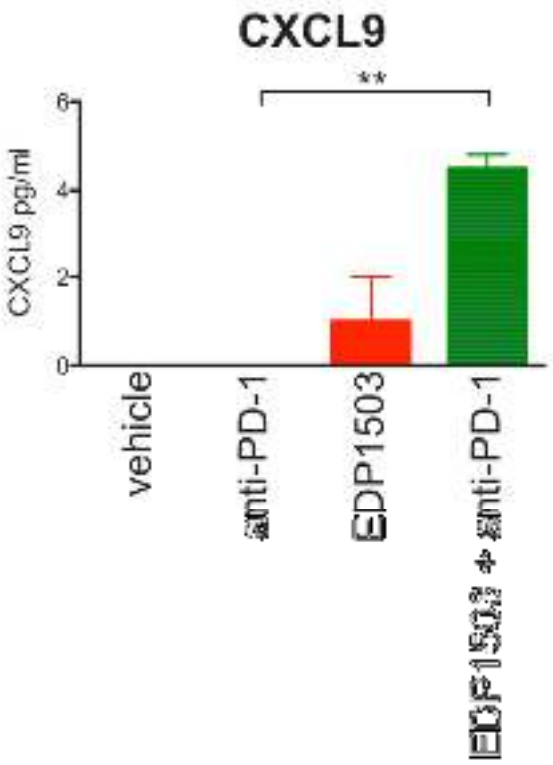


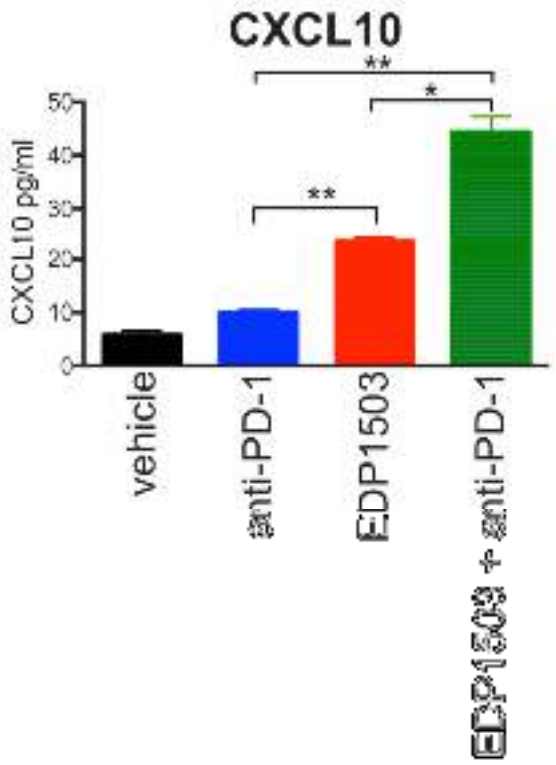
NK And T Cell Infiltration Correlate with Reduced Tumor Growth

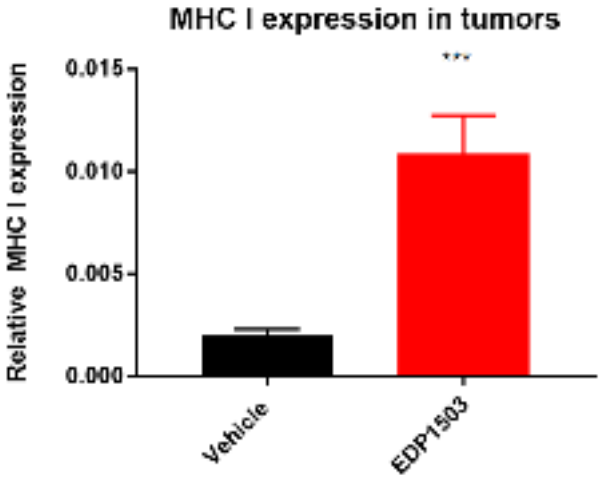


Data from CT26 tumors at Day 7 post-treatment

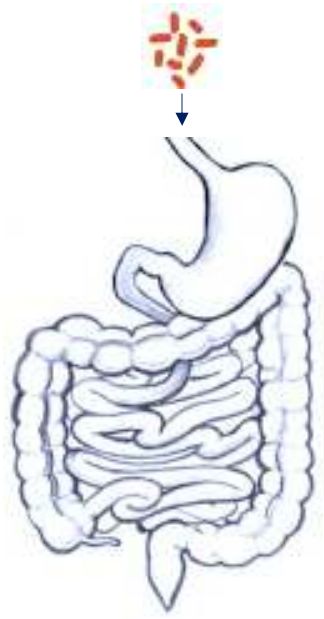
EDP1503 Induces CXCL9/10 and MHC Class I in the Tumor







EDP1503 Modulates Multiple Anti-tumor Immune Mechanisms



Clinically validated mechanisms of tumor immune stimulation	Component of mechanism of EDP1503
Upregulation of antigen presentation	Yes
Control of M1/M2 balance	Yes
Influx and activation of NK cells	Yes
Activation of dendritic cell influx and cross-presentation	Yes
Active chemoattraction and expansion of CD8 effector cells	Yes

EDP1503 Clinical Trials Underway:
Multiple Cancer Types in Combination with pembrolizumab

Overview:	Open label safety, tolerability and efficacy studies of EDP1503 in combination with a checkpoint inhibitor
Endpoints:	Safety and tolerability Overall response rates Biomarkers of immune response in tumor biopsies
Dosing:	Daily oral administration; single dose

EDP1503 Melanoma University of Chicago IST

Timeline: Initiated in January 2019; clinical data H2 2020

Checkpoint naïve patients

EDP1503 Monotherapy → **EDP1503 + pembrolizumab**

PD-1/L1 relapsed patients

EDP1503 Monotherapy → **EDP1503 + pembrolizumab**

2 weeks (w/ paired biopsies)

N= ~70

EDP1503 Evelo-sponsored trials, clinical collaboration with Merck

Timeline: Initiated in Q4 2018; clinical data H1 2020

MSS CRC

EDP1503 Monotherapy → **EDP1503 + pembrolizumab**

2 weeks

Triple-negative Breast Cancer

EDP1503 Monotherapy → **EDP1503 + pembrolizumab**

2 weeks

Relapsed responders: bladder; GE; RCC; MSI; NSCLC

EDP1503 Monotherapy → **EDP1503 + pembrolizumab**

2 weeks

N= ~100

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10 Diversified Clinical Readouts Expected Across 2019 and 2020

	Product Candidate	Indication	Preclinical Development	Phase 1	Phase 2	Phase 3	First Subject First Dose (Expected)	Initial Clinical Readout (Expected)
INFLAMMATION	EDP1066	Atopic Dermatitis		Phase 1b			Initiated	2Q 2019
	EDP1066	Psoriasis		Phase 1b			Initiated	2Q 2019
	EDP1066	Inflammation[1]					2H 2019	2H 2020
	EDP1815	Atopic Dermatitis		Phase 1b			Initiated	2H 2019
	EDP1815	Psoriasis		Phase 1b			Initiated	2H 2019
	EDP1815	Inflammation[1]					2H 2019	2H 2020
ONCOLOGY	EDP1503	MSS Colorectal Cancer[2]		Phase 1/2			Initiated	1H 2020
	EDP1503	Triple-negative Breast[2]		Phase 1/2			Initiated	1H 2020
	EDP1503	Anti-PD-1 Relapsed[2]		Phase 1/2			Initiated	1H 2020
	EDP1503	Checkpoint Naïve Melanoma[3]		Phase 2a			Initiated	2H 2020
	EDP1503	Checkpoint Relapsed Melanoma[3]		Phase 2a			Initiated	2H 2020

[1] We expect to advance EDP1815 and EDP1066 into additional inflammatory disease indications in the second half of 2019. We intend to finalize the indication selection decisions after data from the ongoing EDP1066 and EDP1815 clinical trails have been analyzed. Potential indications include asthma, psoriatic arthritis, rheumatoid arthritis and inflammatory bowel disease.

[2] The Phase 1/2 study of EDP1503 in combination with KEYTRUDA is being conducted in a clinical collaboration with Merck.

[3] The Phase 2a study of EDP1503 in combination with KEYTRUDA in melanoma is being conducted in an investigator-sponsored study by the University of Chicago.

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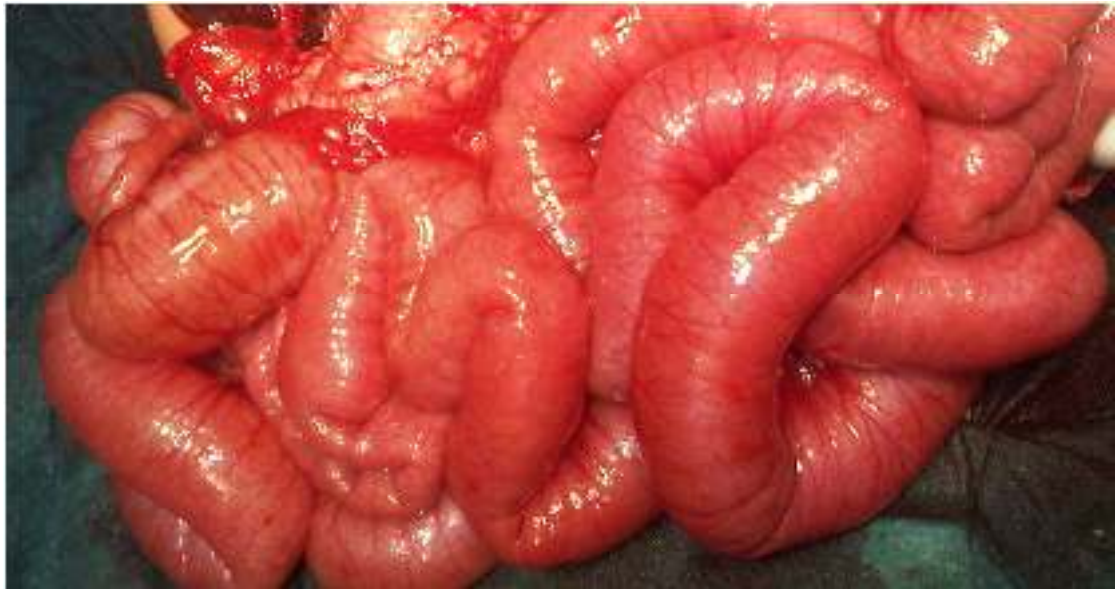
"Nothing in biology makes sense except in the light of evolution."

Theodosius Dobzhansky




ADD MICROBES