Evaluate Vantage

February 21, 2017

Asco-SITC – Oncology could give gutsy biotechs another chance

Jacob Plieth

Companies focusing on the gut microbiome were dealt a serious blow last year with Seres's phase II failure, but now a small study could reinvigorate the field. The trial looks like the first to show in humans that response to the anticancer checkpoint blockade could be determined by the composition of patients' gut bacteria.

Most biotech start-ups in this field have focused on more obvious applications, like treating bacterial and gastrointestinal diseases – strategies that have brought in over $600m of financing (see table below). But immuno-oncology offers a new avenue, and two players, Synlogic and Evelo Biosciences, already have an early focus here.

Of course, a link between the microbiome – the genetic makeup of the microbes in the human body – and diseases from asthma to multiple sclerosis has been postulated for some time. But its role in cancer immunotherapy, while intriguing, was a very early hypothesis.

Indeed, the only recent evidence backing it had come from the University of Chicago's preclinical trial, which showed that introducing *Bifidobacterium sp* bacteria into the digestive tracts of mice with melanoma resulted in an anticancer effect comparable with checkpoint inhibitor treatment.

Human trial

Now a new study, from researchers at the University of Texas MD Anderson Cancer Center, appears to back up the theory with human data; the scientists say theirs is one of the first trials to explore the association between the microbiome and immunotherapy responses in people.

It involved retrospective analysis of over 200 faecal and oral microbiome samples from advanced melanoma patients who went on to receive therapy. The most interesting concerns 43 patients who got PD-1 inhibitors, 30 of whom responded and 13 of whom did not.

Analysis of their faecal samples revealed a greater abundance of *Ruminococcus sp* bacteria in the guts of responders, while non-responders had relatively greater numbers of bacteria from the order Bacteroidales. The results were presented yesterday at the first Asco-SITC Clinical Immuno-Oncology Symposium, in Florida.

Meanwhile, density and abundance of *Faecalibacterium* species was linked to tumour infiltration with immune cells, which itself is a known predictor of response. Interestingly, there was no association between oral microbiome composition and response.

The research could be especially interesting to Synlogic and Evelo, two private microbiome start-ups that already have a stated focus on cancer. Other players exploring the role of gut bacteria could also find in the data a reason to turn to oncology after Seres's failure to treat *Clostridium* infection (*Seres failure a kick in the gut to microbiome field, August 1, 2016*).

And it could be that venture financiers start to view oncology as ripe for investment – they have already pumped vast sums into non-oncology microbiome-focused businesses.

Selected microbiome-focused companies		
Company	**Focus**	**Total financing**
Seres Therapeutics	*C diff* infection (phase II failure)	$69m VC funding plus $134m IPO
C3J Therapeutics	Antimicrobials	$118m
Synlogic	Rare disease & immuno-oncology	$74m
Second Genome	Inflammatory bowel disease	$63m
Vedanta Biosciences	Autoimmune & inflammatory disease	$50m
Kallyope	Central nervous system	$44m
Enterome	Crohn's disease	$40m
Evelo Biosciences	Oncology	$35m
Rebiotix	*C diff* infection	$30m
Eligo Bioscience	Antimicrobials	$2m

Obviously, major caveats of the MD Anderson trial are that it was retrospective and of a limited size. The next stage would be to test the theory prospectively – such a study run by the Parker Institute for Cancer Immunotherapy is to start this year – as well as to investigate the role of faecal transplants on response.

The researchers also speculate that antibiotics could in future be used to deplete some deleterious bacteria – like Bacteroidales, presumably. As for the mechanisms through which gut bacteria enhance anticancer responses, the University of Chicago group speculates that *Bifidobacterium* interacts with roaming dendritic cells and promotes antigen presentation.

However, this still needs to be investigated further, say the MD Anderson researchers, and more work is needed to understand how the microbiome can be tweaked so more cancer patients benefit from immunotherapy. Perhaps this is where industry and VC funds step in.

To contact the writer of this story email Jacob Plieth in London at jacobp@epvantage.com or follow @JacobPlieth on Twitter