

**Microbiome Yarns: *Bifidobacterium*, human milk oligosaccharides, synthetic biology and spooks<sup>1,2,3</sup>**

*Kenneth Timmis<sup>#</sup> and Franziska Jebok<sup>°</sup>, <sup>#</sup>Institute of Microbiology, Technical University Braunschweig, Germany and <sup>°</sup>Institute for Educational Science, University of Freiburg, Germany*

*Friday evening, 5.35pm, in the main bar of the Bulls and Bears in the City (London), a favourite watering hole of Financial Masters of the Universe<sup>4</sup> and would-be EMUs:*

*Bondage, nonchalantly leaning against the bar: Hi, I guess that the red carnation you are sporting indicates that you are the gentleman from Menacyn. Bondage, at your service!*



*von-Spectre: My goodness, public schoolboys are indeed forward!*

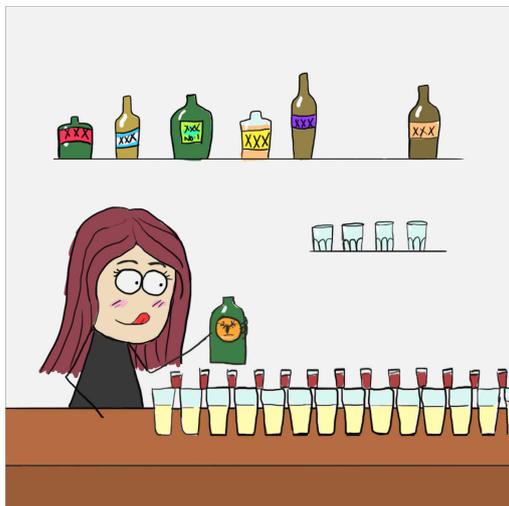
*Bondage: Very droll! My name is Bondage, James Bondage.*

*von-Spectre: Sorry, unable to resist! Good evening James, my name is Mamba von-Spectre, but you can call me Mam. Shall we sit in that inconspicuous corner over there where everyone can see us but, with this happy hour noise, no-one can hear us. Let us have a drink – my friends checked this place out in advance and it seems to be reasonably safe.*

*Bondage: Sure – let's have a Jäger-Train<sup>5</sup> between us; then we can be reasonably sure that our drink does not contain anything untoward.*

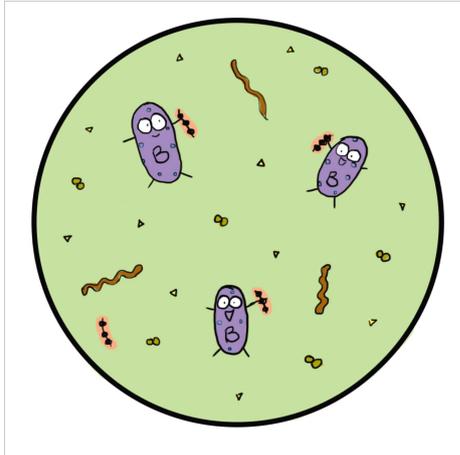
*von-Spectre: Good idea. Miss! We'd like a Jäger-Train – a 20-er should initially suffice.*

*A few minutes later, after chairs around the corner table are re-, and re-, and re-arranged to provide both with adequate lines of sight to the multiple entrances and other doors:*



*Bondage:* So Mam... what does Menacyn have in mind this time that requires the attention of Her Majesty's Secret Service?

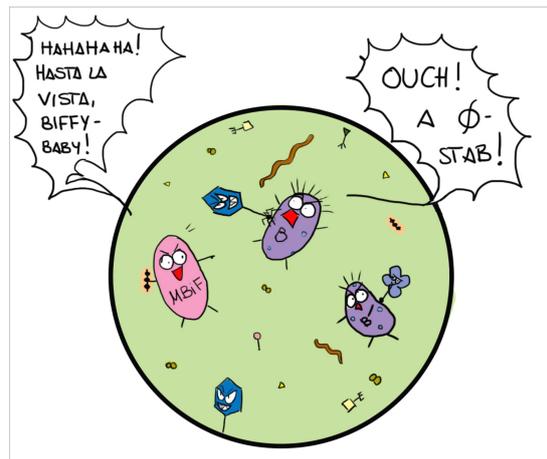
*von-Spectre:* Ah, James – you always get straight to the point, unlike the fetching and ever-so diplomatic Miss Geld-Groschen... HM Secret Service, did you say? MIH57<sup>6</sup> is more like HM *Unsecret* Service, after our friends at Wackidribbles did their public-spirited work. Ok, just a bit of background to put you in the picture. As you are almost certainly aware, recent research has shown that human milk contains a remarkable number of a type of compound called human milk oligosaccharides, or HMOs, which, unexpectedly, do not nourish the baby, but instead serve as food for a bug called *Bifidobacterium infantis*, or Bif for short<sup>7</sup>. Breast feeding thus provides a continual selective advantage for Bif, which has otherwise to compete with other bugs that ordinarily colonise the infant intestine. The thing is this: Bif, unlike these other bugs, orchestrates correct development of the immune system and provides protection against some infections. Cow's milk, though nutritious for infants, does not select for Bif, and the other bugs that colonise the infant intestine are not nearly as effective at building an effective immune system.



Without Bif in infancy, people are less effective at handling infections and are more prone to develop allergies. Are you following me?

*Bondage:* Of course – this is common knowledge.

*von-Spectre:* Good! What is not common knowledge is that Menacyn scientists have developed an anti-Bif virus cocktail that kills all known variants, except one, a designer Bif



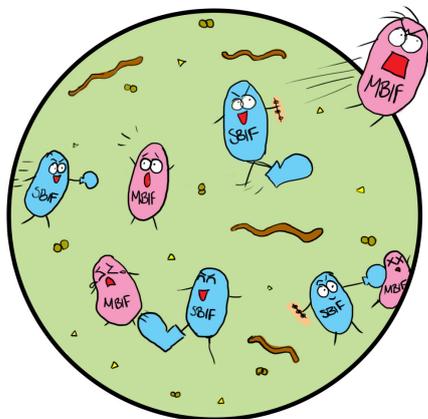
we have named Menacynbif, which can only grow when provided with a secret baby formula we have developed in parallel. We have packaged the phage cocktail in a microcapsule that ensures virus survival under all the different conditions that might be encountered in the various routes we plan for delivery, but that dissolves in the intestine to release the virus. Without Bif, the world will become highly susceptible to mild common infections, like flu.

*Bondage:* Interesting... and I daresay that Menacyn has done all this for a reason that you would like to communicate to HM Government?

*von-Spectre:* Exactly; that is the purpose of this evening's *tête-a tête*, or Jäger-Train... shall we order another? Miss: same again, please!

As I was saying, we have the wherewithal to create health havoc among populations of the world lacking access to Menacynbif. We now propose to offer HMGov access to Menacynbif in return for the totality of its currency reserves, including the rather pathetic amount of gold remaining after the catastrophic fire sale in the late 90s-early 00s. Since Menacynbif requires certain secret nutrients, and dies without them, it will also be necessary to enter into an irrevocable 100-year contract to purchase a national supply annually. The alternative is health chaos for HM subjects and the enormous economic burden – healthcare and productivity loss – that would ensue which, believe me – we have done the health economic evaluation<sup>8</sup> calculations – would greatly exceed the cost of access to Menacynbif.

*Bondage:* Okay, so that is the game. Unfortunately for you, Mam, and your Menacyn cronies, MIH57 anticipated all this ages ago and has a neat defence in the drawer. Let me enlighten you with a little bit of the story. Some years ago, we commissioned the development of a purely synthetic, genetically-stripped down version of Bif, called Synbif, which has all the desired immune stimulating properties of Bif, but is entirely resistant to all known phages. The microbiologists who developed Synbif – a strategic alliance between the Lorenzo von Syntech High Security Institute for Artificial Life in Madrid, and a secret



high-tech germ warfare defence group, reportedly located at Porton Up! – also engineered into it a couple of properties that make it super competitive, such that, when ingested, it eliminates all other Bif strains. If and when necessary, Synbif can be deployed anywhere in the world to eliminate Menacynbif, and thereby neutralise any security threat represented by Menacynbif for the UK and its allies. Synbif, like Menacynbif, also has specific nutritional requirements that must be delivered as a dietary supplement, so it can itself be easily eliminated at any point after deployment, once the all-clear is given, and Bif can safely return to normal duty.

*von-Spectre:* Well done James! A wonderful impromptu story! But: to have something like this, you would have had to have done some pretty serious human trials that would not have gone unnoticed, so I am rather sure that Synbif is a figment of your imagination.

*Bondage:* Well, Mam, you can of course believe whatever you wish, but I suppose that your Menacyn superiors will be at least a little nervous. And... just to make them a tad more nervous, I'll give you a little more intelligence. Three secret trials were indeed carried out: one by us on a well-populated island off HM coast, and subsequently two of our Southern European allies each carried out a trial on one of their offshore islands. Obviously, the results have not been published, but all trials were successful.

*von-Spectre:* This also does not appear credible: the famed transparency of the democratic British system would have created an uproar, so I cannot imagine HMGov wanting to run the risk of an adverse public reaction.

*Bondage:* Actually old sport, HMGov is not always as transparent as one might imagine and, since the folks on the island in question pay very little tax, and thus have little clout with HMGov, MIH57 was not too concerned. So, actually I think it is Menacyn that is now on the back foot. It seems that we might have yet again achieved stalemate.



Miss! Please bring us that bottle of 1990 Romanée-Conti I asked you to order for this evening: we both need to re-educate our palates!

*Bar person:* Sorry, Sir: your favourite wine purveyor in St. James's Street has run out of the 1990 vintage and could only provide the 1989.

*Bondage:* Dinna worry lass, the 1989 is also reasonably drinkable and will save HMGov about a grand.

## Acknowledgements

We are grateful to Jack Gilbert and Victor de Lorenzo for their encouragement, but any inaccuracies, excesses or instances of poor taste are entirely the fault of the authors

## Notes

<sup>1</sup>**Health Warning.** This article is a figment of the authors' imagination; any serious contemplation may be harmful to mental health.

<sup>2</sup>Any possible resemblance to individuals or organisations, real or fictional, is entirely coincidental and unintended

<sup>3</sup>Dedicated to the pioneering researchers who are figuring out what HMOs do and what their consequences are, and to mothers who persist with breastfeeding whatever difficulties experienced, to equip their babies with the best immune system possible.

<sup>4</sup>Masters of the Universe: see *The Bonfire of the Vanities* by Tom Wolfe

<sup>5</sup><https://www.youtube.com/watch?v=6rMFNiDRrKg>

<sup>6</sup>a comprehensive reorganisation of the MI6 (Military Intelligence Section 6), following exposure of many of its operatives by Wackidribbles and subsequent hacking attacks from 8-year old children at a primary school in Aldershot, resulted in its breakup into multiple small, unconnected cells with MI designations reflecting favourite military meals.

<sup>7</sup>e.g. Schell, M. A., et al. 2002. The genome sequence of *Bifidobacterium longum* reflects its adaptation to the human gastrointestinal tract. *Proc. Natl. Acad. Sci. USA* 99: 14422-14427; Underwood, M. A., et al. 2015. *Bifidobacterium longum* subspecies *infantis*: champion colonizer of the infant gut. *Pediatr. Res.* 77: 229-235.

<sup>8</sup>Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes*. 4th ed: Oxford: Oxford University Press; 2015