Predicting safe sandwich production

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Overall, these results suggest that lower concentrations of peptidomimetics could be applied in subsequent in vivo trials as compared to laboratory based MIC determinations. At a clinical level, this may provide an innovative tool for treatment optimization of nosocomial bacterial infections.

P13: Competition enhances the relative fitness of a preformed aggregate in *Pseudomonas aeruginosa* biofilm development

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The establishment of a biofilm in a new habitat has for decades been defined as single cells seeded on a surface. However, colonization of new niches is not solely achieved by single cell dispersal from biofilm upstream; sloughing of large aggregates can colonize as well. To investigate the role of these aggregates in early biofilm development, we used continuous flow systems and in silica simulations. Pre-formed aggregates had a profound local effect on the development of a biofilm. It was observed that initial cell density depends on the relative fitness of aggregates compared to single cells on the surface. In addition, higher competition for resources on the surface increases the relative fitness for aggregates as a result of the heterogeneous growth pattern of aggregates. By elevating certain populations, it was observed how the top of aggregates are able to access nutrients, unavailable to the surface population. We hypothesize that aggregate colonization is a naturally occurring event, which gives the aggregating population an advantage over single cells in niches with high competition. This would occur by being able to access untapped resource in the laminar flow above the resource consuming layer of cells on the surface. An aggregate's geometric shape and heterogenic growth pattern may be an example of kin selection, by a central population sacrificing growth to place its top cells in a favorable position. This confers to the aggregate a resilience towards sudden changes in the local environment and an opportunity to establish itself in a competitive system with a laminar flow over a surface.

P14: A model for chronic fungal and poly-microbial osteomyelitis in mice

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Osteomyelitis and implant infections are severe diseases, which cost the healthcare system millions of kr. each year. The most resent studies show that about 5% of implants fail with between 2 and 25% of these being caused by infection. With a general population of increasing age, medical and technological advances the amount of implant surgeries is estimated to increase dramatically over the next decades. In osteomyelitis *Staphylococcus aureus* is the main cause of the infection, while for implant infections the most common etiological agents are Gram-positive bacteria like *S. aureus*, *S. epidermidis* and *Propionibacterium acnes*. While infections with Gram negative bacteria do occur, they account for a significantly lower number of cases. One of rarest causes of implantitis and osteomyelitis are fungi, specifically the *Candida* species. While very rare, they often affect patients with compromised immune systems causing severe morbidity and high mortality rates. Because of the lack of animal models, current treatment regimes are evaluated based on previous cases for testing and treatment optimization.

We herein show that establishment of an at least 10-day chronic fungal osteomyelitis is possible in a mouse model. This is without the use of immune suppressants to sustain the infection. Furthermore, we show that *C. albicans* and *S. aureus* have a synergistic effect on each other and the pathology of the disease. However, more work is needed as the initial study population is lacking in order to say anything of statistical relevance. Furthermore, the Shirtliff group has been typing the immune response in a similar *S. aureus* model, and it would be interesting to compare that data with *C. albicans* alone and with *C. albicans* and *S. aureus* data.

P15: Predicting safe sandwich production

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Time and temperature control is crucial to avoid growth of pathogens during production and serving of cold ready-to-eat meals. The Danish guidelines state that chilled foods, such as sandwiches, should not be outside the cold chain for more than 3 hours including the time for preparation and serving. However, Danish sandwich producing companies find it challenging to comply with this and have expressed a need for more flexibility. The Danish guidelines do allow for a prolongation of the acceptable time outside the cold chain, if the safety of the specific production can be documented. There is, therefore, room for developing targeted tools for evaluating the time-temperature scenarios in sandwich production. This study describes a decision support tool developed to offer the producers more flexibility. Based on time/temperature measurements obtained during preparation combined with information on the prehistory of ingredients and the expected time/temperature conditions of distribution and serving, the potential growth of *Listeria monocytogenes*, Salmonella and psychrotrophic *Clostridium botulinum* in the sandwiches is predicted. Applying the lag times of these pathogens as the critical limit, the tool determines if the sandwich production is safe by evaluating whether any of the lag times have been exceeded during the total preparation, distribution, and serving time. The growth models employed were built as part of the study using a "worst case" ingredient.

P16: The antibacterial compound tropodithietic acid effects iron metabolism in *Escherichia coli* MG1655

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Tropodithietic acid (TDA) is produced by some marine bacteria. It has a broad antibacterial effect and resistance to TDA does not evolve easily. Also, TDA has a very low toxicity in eukaryotic models (*C. elegans* and Artemia). The purpose of this study was to investigate the transcriptome of TDA-exposed *E. coli* to determine the mechanism of action and the general physiological response caused by TDA-related stress. Exponentially growing *E. coli* MG1655 cells were exposed to sub-lethal concentrations of TDA and sampled after 30 and 60 min. Total RNA was isolated, cDNA library constructed and sequenced. Thirty-six genes involved in iron homeostasis were up-regulated after 30 min of TDA exposure including genes encoding siderophores and transporters of siderophores and ferrous iron. This is indicative of iron limitations within the cell and TDA can indeed chelate iron. In contrast to expected, *E. coli* became more sensitive to TDA the more iron (FeCl3, FeSO4 or hemin) was added to the MIC assay, indicating that TDA bound to iron also has an antibacterial activity. Scanning electron microscopy revealed that TDA caused pore-like formation in *E. coli*, however, divalent cations did not protect the cells from TDA. Therefore, membrane damage is probably not the primary target of TDA. It is possible that TDA has multiple targets, and this is why resistance and tolerance has not been observed.

P17: Antibiotic treatment affects intestinal permeability and gut microbiota in female Wistar rats dependent on antibiotic class

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Introduction. Antibiotics are used for treating bacterial infections. During antibiotics administration the gut microbiota is often affected. This may subsequently affect intestinal integrity and host health.

Methods. Female Wistar rats (n=60) were dosed with amoxicillin (AMX), cefotaxime (CTX), vancomycin (VAN), metronidazole (MTZ), or water (CON) every day for 10-11 days (n=12 in each group). Changes in bacterial composition in faecal and caecal content were determined by partial sequencing of the 16S rRNA gene. Intestinal permeability was determined in vivo by measuring permeability of 4kDa FITC-dextran.