

## Review on Virulence Factors Commonly Used for Animal Nutrition

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### Description

The chromosome and plasmid encode 7914 and 80 proteins, respectively. In addition, we found that catalases were more abundant in human isolates. Furthermore, we also found no significant differences in the proteins between different strains from different sources. The pan-genomic analysis also showed that 67 genes could only be found in humoral isolates. The composition of unique genes in humoral isolate genomes indicated that the transcriptional regulators may be important when *Nocardia* invades the host, which allows them to survive in the new ecological system.

### Biomaterials Design

Novel biomaterials designed to enhance tissue regeneration can bring new opportunities to advance the effectiveness of surgical procedures. Surgical procedures have a traumatic effect on micro vessels that reduces the blood supply to healed tissues. Sufficient nutrient and oxygen supply is a key factor for collagen synthesis. Resulting shortage of collagen in regenerating tissue leads to weaknesses that could lead to serious postoperative complications.

One of the most serious postoperative complications after an intestinal anastomosis is an anastomotic leak a defect in the intestinal wall and possible entry point for infection resulting in potential sepsis, multi-organ failure and even death. The most problematic parts of the gastrointestinal tract are the large intestine and the rectum as they have the highest leakage rate, the slowest healing rate and decreased collagen content in healed tissue. Healed anastomoses with lowered collagen content have less mechanical strength and are more prone to leakage. Hence, a potential way to increase the tensile strength of intestinal anastomoses and to reduce leakage rate seems to be to provide support for collagen-producing cells, hence stimulating collagen production.

For cells producing collagen, being adhered to the Extracellular Matrix (ECM) is vital. Without sufficient cellular adhesion to the ECM, the cells will not be able to proliferate and produce collagen. Therefore, the discontinuity and shortage of ECM at the site of a surgical wound would create a need for a material that would help cells to attach, proliferate and produce further ECM. The material should mimic the structure and functions of ECM. Electro spun nanofibers seem to be a suitable

material providing optimal cell adhesion leading to cell proliferation and production of ECM.

### Infected Animal Death

In this study, we confirmed that NT001 could cause infected animal death, and identified many possible virulence factors for our future studies. This study also provides new insight for our further study on *Nocardia* virulence mechanisms. A current topic interest in regenerative medicine is the development of novel materials for accelerated healing of sutures, and nanofibers seem to be suitable materials for this purpose. As various studies have shown, nanofibers are able to partially substitute missing extracellular matrix and to stimulate cell proliferation and differentiation in sutures. Therefore, we tested nanofibrous membranes and cryogenically fractionalized nanofibers as potential materials for support of the healing of intestinal anastomoses in a rabbit model.

We compared cryogenically fractionalized chitosan and PVA nanofibers with chitosan and PVA nanofiber membranes designed for intestine anastomosis healing in a rabbit animal model. The anastomoses were biomechanically and histologically tested. In strong contrast to nanofibrous membranes, the fractionalized nanofibers did show positive effects on the healing of intestinal anastomoses in rabbits. The fractionalized nanofibers were able to reach deep layers that are key to increased mechanical strength of the intestine. Moreover, fractionalized nanofibers led to the formation of collagen-rich 3D tissue significantly exceeding the healing effects of the 2D flat nanofiber membranes. In addition, the fractionalized chitosan nanofibers eliminated peritonitis, significantly stimulated anastomosis healing and led to a higher density of microvessels, in addition to a larger fraction of myofibroblasts and collagen type I and III. Biomechanical tests supported these histological findings.

We concluded that the fractionalized chitosan nanofibers led to accelerated healing for rabbit colorectal anastomoses by the targeted stimulation of collagen-producing cells in the intestine, the smooth muscle cells and the fibroblasts. We believe that the collagen-producing cells were stimulated both directly due to the presence of a biocompatible scaffold providing cell adhesion, and indirectly, by a proper stimulation of immunocytes in the suture.

Actinobacteria belong to a phylum of Gram-positive bacteria that provide important contributions to soil systems. Many actinobacteria are branched and always grow extensive mycelia. According to their special characteristics, most of actinobacteria are important in bioproducts synthesis, including immunosuppressive compounds, cytostatic and antibiotic. Both mycobacteriaceae and nocardiaceae belong to corynebacterineae, and can produce mycolic acids, which can help pathogens resistant to the attack of hosts.

Nocardia belongs to nocardiaceae family, which can cause immune compromised patient diseases. The genus of nocardia is

gram-positive and catalase positive and comprises aerobic bacteria that belong to actinobacteria. Corynebacterium, mycobacterium and nocardia form the well-known CMN action bacterial group. Similar to other actinobacteria, mycolic acids in the cell wall represent one of the important structures of nocardia, making them act as partially acid-fast bacteria. Nocardia is not a commensal bacterium, and was first described by Edmond Nocard in 1888. With the rising number of immune compromised patients, nocardiosis incidence has recently increased, but the pathogenic mechanisms of nocardiosis are still unclear.