Seminar #8

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Polymersomes eradicating intracellular bacteria

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Mononuclear phagocytes such as monocytes, tissue-specific macrophages, and dendritic cells are primary actors in both innate and adaptive immunity. These professional phagocytes can be parasitized by intracellular bacteria, turning them from housekeepers to hiding places and favoring chronic and/or disseminated infection. One of the most infamous is the bacteria that cause tuberculosis (TB), which is the most pandemic and one of the deadliest diseases, with one-third of the world's population infected and an average of 1.8 million deaths/year worldwide. Here we demonstrate the effective targeting and intracellular delivery of antibiotics to infected macrophages both in vitro and in vivo, using pH-sensitive nanoscopic polymersomes made of PMPC–PDPA block copolymer. Polymersomes showed the ability to significantly enhance the efficacy of the antibiotics killing Mycobacterium bovis, Mycobacterium tuberculosis, and another established intracellular pathogen, Staphylococcus aureus. Moreover, they demonstrated to easily access TB-like granuloma tissues — one of the harshest environments to penetrate — in zebrafish models. We thus successfully exploited this targeting for the effective eradication of several intracellular bacteria, including M. tuberculosis, the etiological agent of human TB. Because of their ability to selectively target human macrophages, PMPC-PDPA polymersomes have been also loaded with Glucocorticoid (GC) drugs to enhance their anti-inflammatory effect in the treatment of Rheumatoid Arthritis. Polymersomes were proved to efficiently promote the inflammation shutdown, while reducing the well-known therapeutic limitations in GC-based therapy.

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