RECHERCHE

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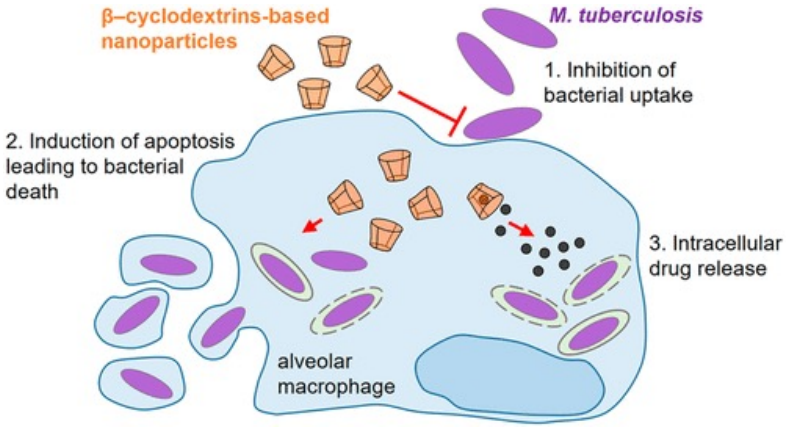
Intrinsic Antibacterial Activity of Nanoparticles Made of β-Cyclodextrins Potentiates Their Effect as Drug Nanocarriers against Tuberculosis

Multi-drug-resistant tuberculosis (TB) is a major public health problem, concerning about half a million cases each year. Patients hardly adhere to the current strict treatment consisting of more than 10 000 tablets over a 2-year period. There is a clear need for efficient and better formulated medications. We have previously shown that nanoparticles made of cross-linked poly-β-cyclodextrins (pβCD) are efficient vehicles for pulmonary delivery of powerful combinations of anti-TB drugs. Here, we report that in addition to being efficient drug carriers, pβCD nanoparticles are endowed with intrinsic antibacterial properties. Empty pβCD nanoparticles are able to impair Mycobacterium tuberculosis (Mtb) establishment after pulmonary administration in mice. pβCD hamper colonization of macrophages by Mtb by interfering with lipid rafts, without inducing toxicity.



Moreover, pβCD provoke macrophage apoptosis, leading to depletion of infected cells, thus creating a lung microenvironment detrimental to Mtb persistence. Taken together, our results suggest that pβCD nanoparticles loaded or not with antibiotics have an antibacterial action on their own and could be used as a carrier in drug regimen formulations effective against TB.

Machelart A, Salzano G, Li X, Demars A, Debrie AS, Menendez-Miranda M, Pancani E, Jouny S, Hoffmann E, Deboosere N, Belhaouane I, Rouanet C, Simar S, Talahari S, Giannini V, Villemagne B, Flipo M, Brosch R, Nesslany F, Deprez B, Muraille E, Locht C, Baulard AR, Willand N, Majlessi L, Gref R, Brodin P.