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PHA-producing bacteria from deep sea environments: Towards a new generation of therapeutics

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Poly-hydroxyalkanoates (PHA) are natural polymers, biodegradable and biocompatible, synthesized by many organisms, especially prokaryotes. There are over 150 kinds of these polyesters, accumulated in a wide variety of bacteria as carbon and energy storage material. PHA granules are deposited intracellularly when microorganisms are cultivated in the presence of an excess of carbon source (carbohydrates, fatty acids etc.) together with a nitrogenous nutrient deficiency. Due to their biodegradability and biocompatibility, PHA can be used as biomaterials in medical or pharmaceutical fields, and numerous therapeutic micro/nano-vectors have already been developed over the past two decades. The present study highlights short and medium chain length PHA (PHAscl-mcl) production capacities of aerobic and mesophilic deep-sea bacteria, isolated during IFREMER cruises from hydrothermal vents in Atlantic and Pacific oceans. According to standardized and optimized fermentation protocols, polymers with original and controlled chemical composition such as poly-3-hydroxybutyrate-co-4-hydroxubutyrate (P3HB4HB) were produced by seven different bacterial genera, including alpha and gammaproteobacteria. Next, PHA has been modified by 'green processes' to obtain amphiphilic copolymers suitable for biomedical use, before grafting onto metal mesoporous nanoparticles. PHA-metal hybrid complex consists of a rigid iron cage, containing drugs or nucleic acids, coated with a protective organic ligand, made of bio based PHA. This new kind of structure allows better cohesion of the vectors in blood flow, internalization in target pathologic cells and improves stealth against the immune system. Finally, these new PHA-metal complexes, responding to drug delivery concept, are intended to increase the therapeutic benefit while minimizing side effects on the human body.

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