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Drug delivery by tattooing to treat cutaneous leishmaniasis

Background: Leishmaniasis is a vector-borne disease that is caused by obligate intra-macrophage protozoa of the Leishmania species. Leishmaniasis can cause different clinical syndromes, including Cutaneous Leishmaniasis (CL), in which the patient generally presents with one or several ulcer(s) or nodule(s) on the skin, resulting from the infection of phagocytic cells located in the dermis. It often results into severe scar tissue in the skin. Most of the twelve million people infected with leishmania worldwide are CL cases, a 1.5 million new cases occur annually.

Objective: WHO has a program to develop new treatments for CL. This study establishes a proof-of-concept that a tattoo device can target intra-dermal drug delivery against CL.

Methods: The selected drug is Oleylphosphocholine (OlPC) formulated as liposomes, particles known to be prone to macrophage ingestion. First is shown that treatment of cultured leishmania-infected macrophages with OlPC-liposomes results in a direct dose-dependent killing of intracellular parasites. Based on this, *in vivo* efficacy is demonstrated using a 10 day tattooing-mediated treatment in mice infected with *L. major* and *L. mexicana*. In both models this regimen results in rapid clinical recovery with complete regression of skin lesions by day 28. Parasite counts and histopathology examination confirm high treatment efficacy at the parasitic level. Low amount of drug required for tattooing combined with fast clinical recovery may have a positive impact on CL patient management.

Results & Conclusion: This first example of tattoo-mediated drug delivery could open to new therapeutic interventions in the treatment of skin diseases. This study demonstrates that the use of a tattoo instrument for drug delivery is possible in the treatment of cutaneous leishmaniasis and that this method can successfully eliminate intracellular parasites at the site of infection. After showing that the selected drug oleylphosphocholine (OlPC) formulated as liposomes could efficiently reach intracellular parasites when in contact with infected macrophages, the activity of the drug was compared *in vivo* in mouse models of old (*L. major*) and new world (*L. mexicana*) leishmaniasis. Three routes of administrations of the same drug formulation were investigated: Systemic (IP) administration, topical administration as a drop and administration via the tattoo instrument. Evaluation parameters included clinical (lesion sizes) and parasitological parameters (burdens) using quantitative and qualitative methods. In all experiments, the tattooing delivery procedure was the most efficacious at both the clinical and parasitological levels.

Biography

Strategic and creative consultant in biomedical science, with a parallel career in the Dutch Civil-Military Interaction Command in which he has responsibility for the counter measures in CBNRe threats and (medical) consequence management both in a military and a civilian (terrorism) setting. He was the director of the 2014 & 2016 World Congress of CBRNe Science & Consequence Management in Tbilisi, Georgia. He works internationally as consultant or scientific supervisory board member for several medical and biotech companies, merely involved in biodefense, clinical diagnostics and therapies. He is also visiting professor for Punjab University in Pakistan and Rhein-Waal University in Germany and visiting professor at the University of Rome Tor Vergata. He has finished both his studies in Medicine and in Biochemistry at the University of Groningen in The Netherlands and has extensive practical experience in cell biology, immuno-haematology, biodefense and transfusion medicine. His natural business acumen and negotiation competence helps to initiate new successful businesses, often created out of unexpected combinations of technologies. His thorough understanding of abstract science combined with excellent skills in the communication of scientific matters to non-specialists, helps him with strategic consulting at top level management.

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