POLY-LACTIDE-CO-GLYCOLIDE MICROSPHERES AND NATURAL PHOSPHOLIPID LIPOSOMES IN THE CONTEXT OF VACCINOLOGY

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The research on new delivery systems within vaccinology has started with the necessity to promote the development of vaccines simpler to deliver than existing ones with particular emphasis on reducing the number of doses needed to induce long-lasting protection. Particular attention has been paid to research on particulate systems with adjuvant and controlled release activities like liposomes and microspheres prepared with biodegradable polymers. We demonstrate here that: when properly manipulate, the immune system produced differentially IgG or IgM (1); the liposome acted as vehicle and adjuvant for the polysaccharide C from \textit{Neisseria meningitides} (2) and the booster timing of PLGA microspheres is determinant factor on increasing antibody titer, neutralizing antibodies and immunological memory (3).

(1) It was observed that the 18hsp (recombinant heat shock protein from \textit{M. Lepra})e, when encapsulated within liposomes, produced preferentially IgG and, when externally exposed, produced IgM in injected mice. To act as adjuvant, the liposome must retain its membrane integrity, here preserved by the action of trehalose. The cryoprotectant action mediated by trehalose is an important improvement on liposome vaccine in the context of hot countries and permits the production of lyophilized vaccines.

(2) The ability of liposomes to act as carriers for the co-encapsulation of B and T epitopes eliminating the need of protein conjugation is a reality. Here the PSC was encapsulated within liposomes containing both 18hsp and ODN1668. The simple encapsulation of PSC within liposomes relieves the presence of both adjuvants the 18hsp (a carrier protein and a source of T epitope) and the ODN1668 (a poly CG motif).

(3) The Dtxd and Ttxd (Diphtheria and Tetanus toxoid, respectively) when encapsulated together, within PLGA [poly (lactide-co-glycolide)] microspheres, enhanced 60 times the antibody production. When the booster was done 120 (instead of 36 days) days after priming the mice, the enhancement of anti-Dtxd and anti-Ttxd were, respectively, 250 and 1024 time greater than the soluble DT vaccine. The same behavior was observed when the neutralizing antibodies were measured. The response patterns and the immune maturity were measured by

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IgG₁ and IgG₂a titrations. It is known that the IgGs are produced in the following order: IgG₁ > IgG₃ > IgG₂a. The neutralizing antibodies are mainly due to IgG₁ (more abundant), but the IgG₂a is more specific and is related to the immunological maturation degree. When the booster were done 111 days after priming the mice produced at least 22 time more IgG₂a than the group that received the booster 44 days after priming. The enhanced of immunogenicity by particulate antigen vehicle was unsurprising, since natural pathogens are also particulate and immune system has evolved to deal with these. The relevant here was the possibility to manipulate the immune system thought timing the booster of vaccines.

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