Exploiting hyaluronic acid as an adjuvant for new anti-tumor preventive and therapeutic vaccination strategies

The use of proteins or peptides as immunogens is attractive for the development of vaccines, especially cancer vaccines, but requires efficient and safe adjuvant formulations to overcome their intrinsic weak immunogenicity. Although dozens of different adjuvants have been shown to be effective in preclinical and clinical studies, alum remains the only one approved for human use in the USA and the most employed worldwide, but it turned out to be inefficient in cancer vaccine formulations. Indeed, the prerequisites for an ideal cancer adjuvant differ from conventional adjuvants. Since cancer vaccines target self-antigens, the ideal cancer adjuvant must be extremely potent to circumvent immune tolerance, but it must also be safe to avoid autoimmune reactions. To solve all these problems, new generation vaccines often incorporate toll-like receptors (TLRs) agonists. Among them, natural polymers that can act as damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs), are emerging as a new efficient class of vaccine adjuvants due to their ability to orchestrate the cross-talk between innate and adaptive immunity.

Prof. Antonio Rosato's team identified low molecular weight (about 200 KDa) hyaluronic acid (HA) as a new safe and effective immunostimulatory adjuvant for protein-based cancer vaccination strategies. HA is a biodegradable, biocompatible, non-toxic, and non-inflammatory biopolymer that has been widely exploited for biomedical and pharmaceutical applications. Moreover, numbers of reports demonstrated that HA fragments can influence dendritic cell maturation (DC) and macrophage activation through stimulation of TLR2 and TLR4. Previous results clearly indicate that only when HA is chemically conjugated to proteins strong humoral and cellular responses were obtained in BALB/c and C57BL6 mice. Notwithstanding, a direct role of HA as adjuvant for cancer vaccine development has never been investigated. To this aim, HA was chemically linked to the extracellular domain of the rat form of the epidermal growth factor receptor (rHER2/neu) and the resulting bioconjugate will be used for immunization of BALB/c mice and transgenic BALB-neuT mice, comparing its adjuvanticity and mechanism of action with alum.