In vivo evaluation of Antibody Recruiting Glycodemdrimers (ARGs) for targeted cancer immunotheraphy

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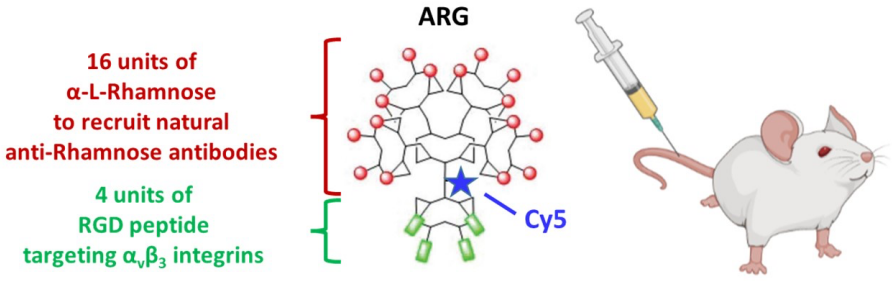
Cancer is a major cause of mortality worldwide and it is estimated that 40% of the population will be diagnosed with cancer within their lifetime. Currently, immunotheraphy with monoclonal antibodies (Abs) has become a promising strategy to fight cancer. However, its use is difficult to standardize, expensive and can lead to intolerable toxicity events. Targeted immunotherapy is an ideal choice to improve cancer treatment.

Over the last fifteen years, synthetic chemistry has allowed the development of bifunctional molecules called Antibody Recruiting Molecules (ARMs). ARMs are composed by a target binding terminus (TBT) able to bind to specific receptors on cancer cells, and by an antibody binding terminus (ABT) able to gather endogenous antibodies. The ternary complex cancer cell-ARG-Abs leads to the activation of different immunological mechanisms and, consequently, to cancer cell clearance without need for previous immunization [1].

In our group, by using supramolecular chemistry, molecular engineering, biochemistry, immunochemistry and glycoscience approaches, we have designed Antibody Recruiting Glycodendrimers (ARGs) bearing four copies of RGD peptide as TBT and sixteen copies of rhamnose as ABT. These ARGs selectively target overexpressed integrins on tumor surface and recruit the natural anti-rhamnose Abs present in human serum [2]. Furthermore, they have also been proved to promote up to 60% of selective cytotoxicity towards cancer cells in vitro [3].

In order to investigate the commercial feasibility and the *in vivo* properties of our lead compounds, we have further investigated ARGs serum stability and blood compatibility *in vitro*, as well as their kinetics, biodistribution and cytotoxic activity *in vivo*. The set of results obtained with these studies would facilitate the transfer of technology and the initiation of clinical development.



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