Design and characterization of oligopeptides capable of interacting with the programmed death ligand 1 receptor for future theragnostic applications

Micaela Giannetti,[1] Marina Gobbo,[2] Isabella Caligiuri,[3] Lucio Litti,[2] Claudia Mazzuca,[1] Flavio Rizzolio,[3,4] Moreno Meneghetti,[2] and Antonio Palleschi[1]
[1]Department of Chemical Science and Technologies, University of Rome "Tor Vergata", and CSGI unit of Rome, Via della Ricerca Scientifica, 00133 Rome, Italy
[2]Department of Chemical Sciences, University of Padova, via F. Marzolo 1, 35131 Padova, Italy.
[3]Pathology Unit, Centro di Rif. Oncologico di Aviano (CRO) IRCCS, via F. Gallini 2, 33081 Aviano (PN), Italy
[4]Department of Molecular Sciences and Nanosystems, Ca' Foscari University of Venice, via Torino 155, 30172 Venice, Italy
micaela.giannetti@uniroma2.it

The programmed death-1 protein (PD-1) present on the membrane of T lymphocytes performs its function only if activated by interactions on its extracellular portion with suitable ligands. PD-L1 (programmed death ligand-1) is a protein placed on the surface of some (regulatory) cells that, by binding to the PD-1 receptor, forms the PD-1/PD-L1 complex and suppresses the immune response against antigens[1].
The interaction is exploited by tumor cells as a strategy to escape the immune system. Indeed, many particularly aggressive tumors, such as melanoma, overexpress PD-L1 on their cells; thus, they manage to deactivate the T lymphocytes, inhibiting the response of the immune system.
In this work, the design and characterization of a new generation of oligopeptides showing a high affinity with the target PD-L1 region able to interact to PD-1 will be presented. Molecular dynamics simulations, supported by experimental data, in solution and on gold surface, suggest that such peptides can compete with the current immunoglobulin and peptide inhibitors[2]. Given the promising results, future studies will consider the appropriate functionalization of gold nanoparticles with these peptides to evaluate their efficacy and selectivity on cancer cells.

[1] Y. Iwai et al. J. Biomed. Sci. 24 (1) (2017) 26
[2] M. Gobbo et al., SERS nanostructures with engineered peptides for targeting the PD-L1 immune checkpoint of tumor cells, submitted.