A Peptide/Fullerene Hybrid for Multivalent Recognition of E-Selectin

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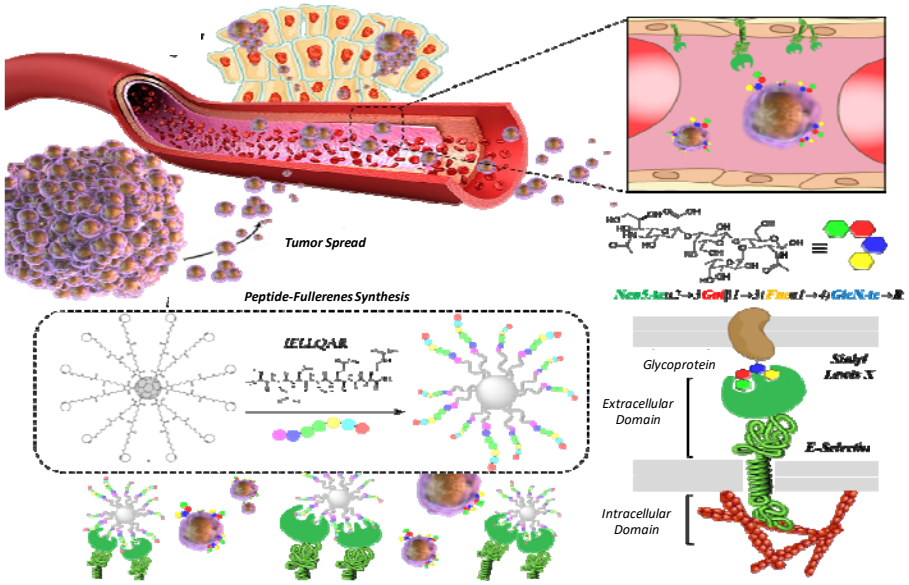
Molecular recognition through ligand-receptor interactions is a very important mechanism for metastatic processes. Among all of them, multivalent protein-carbohydrate interactions play a fundamental role in tumor cell-endothelial cell recognition processes. In particular, the interaction between SLex and SLea expressed in circulating tumor cells and proteins of the family of selectins, overexpressed in endothelial cells. Unlike tumor cells, vascular endothelial cells receptors are a stable target not subjected to genetic modifications. In addition, the elimination of a single endothelial cell involves the death of hundreds of tumor cells. Targeting endothelial receptors cells offers a high potential in tumor diagnosis and therapy.



SLex and SLea are the natural ligands of selectins, but their complicated chemical synthesis and their low affinity for selectins made difficult to continue with their development. Recently, through "phase display" it was identified a simple peptide with a linear sequence of seven amino acids (Ile-Glu-Leu-Leu-Gln-Ala-Arg) called IELLQAR that interacts specifically with selectins. IELLQAR is a very simple compound, which can be synthesized using SPPS. IELLQAR can be functionalized and easily conjugated to fullerenes for its multivalent presentation. In addition, it can be combined with diagnostic and therapeutic agents.

References

[1] Smith, B. A. H.; Bertozzi, C. *Nat. Rev. Drug Discov.* **2021**, 20, 217.243.

[2] Fukuda, M. N. et al. *Cancer Res.* **2000**, 60, 450-456

[3] (a) Ramos-Soriano, J. et al. *Chem. Commun.* **2016**, 52, 10544-10546; (b) Ramos-Soriano, J. et al. *J. Org. Chem.* **2018**, 83, 1727-1736.