CYCLE DE CONFÉRENCES DE CHIMIE

Avec le concours de : Université Clermont Auvergne
INP Clermont Auvergne

Jeudi 17 décembre à 16 h

Salle C (site des Cézeaux)

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Exploiting Multivalency in Molecular Recognition: From Peptide Vectors to Antibody-Inspired Solutions

Multivalency is central to biological systems, enabling molecular recognition, cellular adhesion, and signal processes. It strengthens interactions between entities like receptors and ligands.[1] In this context, we design bioinspired multivalent biomolecular compounds for several applications. Access to such compounds may become a challenging task. We then developed methodologies using chemoselective ligations to achieve sophisticated macromolecules with desirable biological properties.[2]

First, we developed peptide vectors targeting protein receptor, such as the $\alpha_V\beta_3$ integrin that is overexpressed in the tumor micro-environment. We have shown that clustered RGD-containing compounds, which target the $\alpha_V\beta_3$ integrin, offer an interesting outlook for biological applications such as tumor imaging, drug delivery and cell capture.[2]

More recently, we designed biomimetic antigen surfaces displaying the CD20 epitope, which is a key target to treat B cell proliferative disorders and autoimmune diseases. Using Label-free technologies (SPR, QCM-D), we have shown that a critical inter-CD20 spacing confers the best conditions for the binding of the monoclonal antibody (mAb) rituximab, thereby improving its biological effect.[3] Today, these surfaces are exploited for the development of rituximab mimics.

Together, these examples show that ligand spacing and relative orientation are critical: multivalent ligand architecture modulates binding affinity, thereby altering biological effects.

References

1 C. Fasting, C. A. Schalley, M. Weber, O. Seitz, S. Hecht, B. Koksch, J. Dernedde, C. Graf, E.-W. Knapp, R. Haag. Multivalency as a Chemical Organization and Action Principle. *Angew. Chem. Int. Ed.* **2012**, *51*, 10472 – 10498.

2 M. Galibert, O. Renaudet, P. Dumy, D. Boturyn. Access to biomolecular assemblies via one-pot triple orthogonal chemoselective ligations. *Angew. Chem. Int. Ed.* **2011**, *50*, 1901−1904.

3 (a) A. Borbély, F. Thoreau, E. Figueras, M. Kadri, J.-L. Coll, D. Boturyn, N. Sewald. Synthesis and Biological Characterization of Monomeric and Tetrameric RGD-Cryptophycin Conjugates. *Chem. Eur. J.* **2020**, *26*, 2602–2605; (b) C. H. F. Wenk, F. Ponce, S. Guillermet, C. Tenaud, D. Boturyn, P. Dumy, D. Watrelot-Virieux, C. Carozzo, V. Josserand, J.-L. Coll. Near-infrared optical guided surgery of highly infiltrative fibrosarcomas in cats using an anti-alpha v beta 3 integrin molecular probe. *Cancer Lett.* **2013**, *334*, 188−195.

4 (a) L. Bar, J. Dejeu, R. Lartia, F. Bano, R. P. Richter, L. Coche-Guerente, D. Boturyn. Impact of Antigen Density on Recognition by Monoclonal Antibodies. *Anal. Chem.* **2020**, *92*, 5396−5403; (b) O. Ricloux, C. Jongwohan, G. V. Dubacheva, L. Coche-Guérente, Q. Laurent, D. Boturyn. Engineered Biomimetic Surfaces Enable Quantitative Profiling of Clustered Cell-Surface Antigens. *Anal. Chem.* **2026**, *98*, 19418–19426.

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