

# TOWARDS NEW CYCLAM-BASED RADIOPHARMACEUTICALS FOR CANCER IMAGING AND THERAPY



**Cédric Ollier<sup>1</sup>, Nathalie Le Bris<sup>1</sup>, Raphaël Tripier<sup>1</sup>**

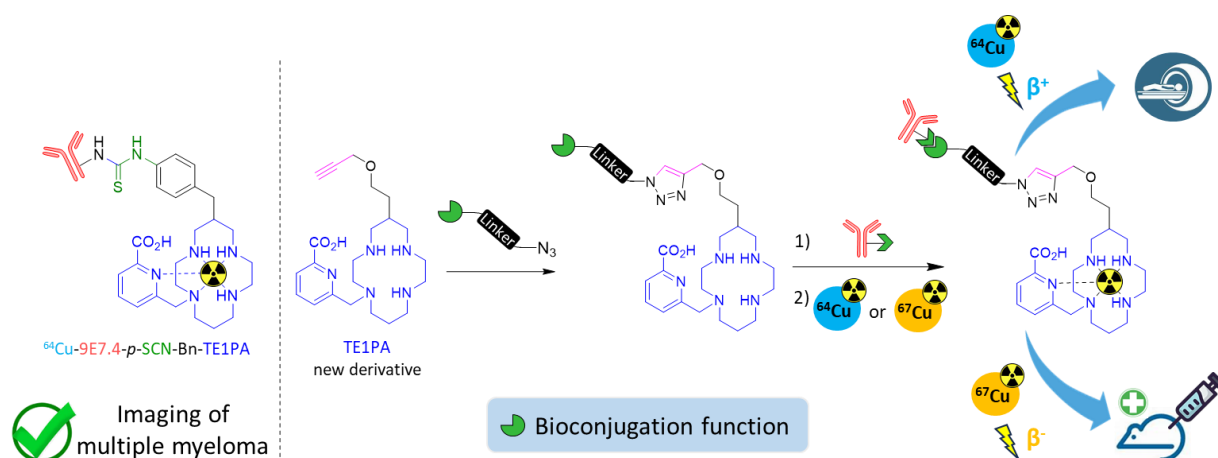
<sup>1</sup>Univ Brest, UMR-CNRS 6521 CEMCA

6 Avenue Victor Le Gorgeu, 29200 Brest, France

cedric.ollier@univ-brest.fr

Polyazacycloalkanes are known for their remarkable chelation properties, especially with cationic metals. Among them, cyclam and its functionalized derivatives have an outstanding affinity with Cu(II), whose copper-64 and copper-67 isotopes are of great interest for cancer imaging and therapy, respectively. In particular, TE1PA, a *N*-picolinate cyclam, forms an extremely stable and inert complex *in vivo* with copper-64.<sup>1</sup> In view of these results, its bifunctional derivative was developed in order to perform further bioconjugation with a monoclonal antibody. This has led to an efficient radiopharmaceutical for multiple myeloma imaging.<sup>2</sup> However, the use of an isothiocyanate as a coupling function is limiting due to a lack of specificity.

In a new investigation step, we have developed a fast and efficient method based on the versatile CuAAC click reaction<sup>3</sup> to synthesize a series of cyclams functionalized by a wide range of functions of interest.<sup>4</sup> This methodology was then used to obtain a new bifunctional TE1PA derivative bearing a more specific bioconjugation function than isothiocyanate, allowing easier development of copper-based radiopharmaceuticals for cancer imaging and therapy.



## References

- <sup>1</sup> Lima, L. M. P.; Esteban-Gómez, D.; Delgado, R.; Platas-Iglesias, C.; Tripier, R., *Inorg. Chem.*, **2012**, 51, 6916.
- <sup>2</sup> Le Bihan, T.; Navarro, A.-S.; Le Bris, N.; Le Saëc, P.; Gouard, S.; Haddad, F.; Gustin, J.-F.; Chérel, M.; Faivre-Chauvet, A.; Tripier, R., *Org. Biomol. Chem.*, **2018**, 16, 4261.
- <sup>3</sup> Meldal, M.; Tornøe, C. W., *Chem. Rev.*, **2008**, 108, 2952.
- <sup>4</sup> Ollier, C.; Méndez-Ardoy, A.; Ortega-Caballero, F.; Jiménez Blanco, J. L.; Le Bris, N.; Tripier, R., *ChemRxiv*, **2023**, DOI: 10.26434/chemrxiv-2023-85pk4.