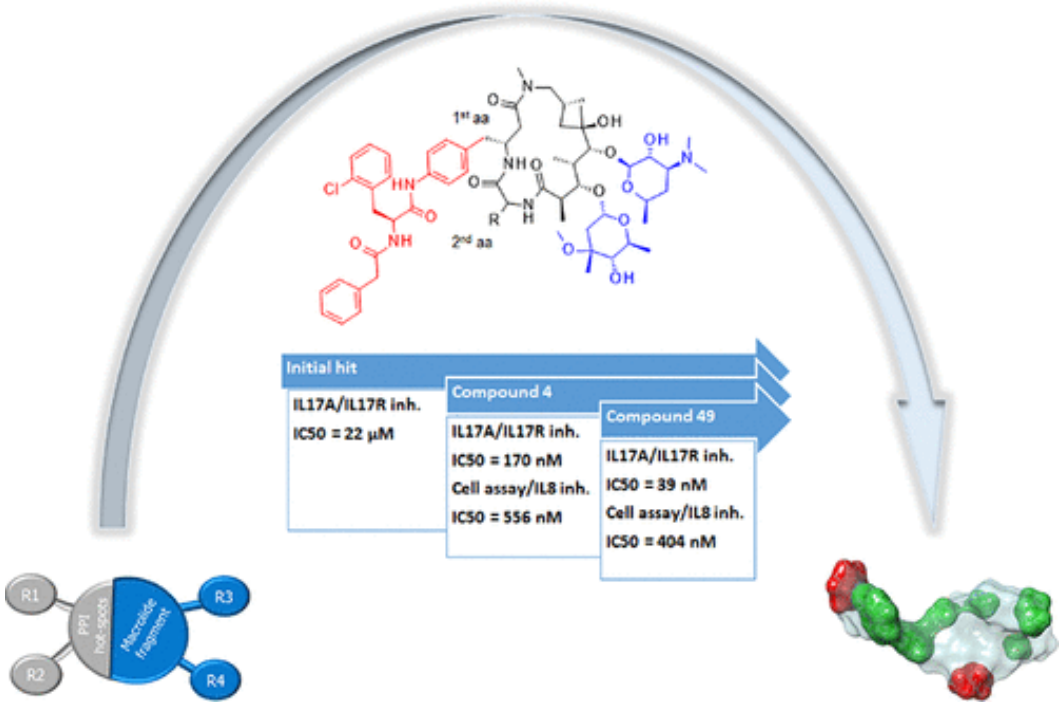
MACROCYCLIC DISRUPTORS: THE NMR SIDE OF THE STORY

Ana Čikoš

Ruđer Bošković Institute, NMR Centre, Bijenička cesta 54, 10000 Zagreb, Croatia
ana.cikos@irb.hr

Interleukin 17A has a significant role in inflammatory response of the body, but also is involved in pathophysiology of autoimmune diseases, such as psoriasis. Protein-protein interactions (PPI) of IL-17A with its receptor IL-17RA are crucial for its activity. Due to their size, PPI targets are very difficult to inhibit using conventional small heterocyclic molecules. The aim of this project was to discover a macrocyclic disruptor which could modulate the IL-17A/IL-17RA binding. This talk is about the role NMR spectroscopy (coupled with computational methods) played at the very beginning of the project which resulted in an nM range inhibitor, as well as the explanation of its binding mode.[1]



REFERENCES

[1] S. Koštrun et al, Macrolide Inspired Macrocycles as Modulators of the IL-17A/IL-17RA Interaction, *J. Med. Chem.* **2021**, *64* (12), 8354–8383.