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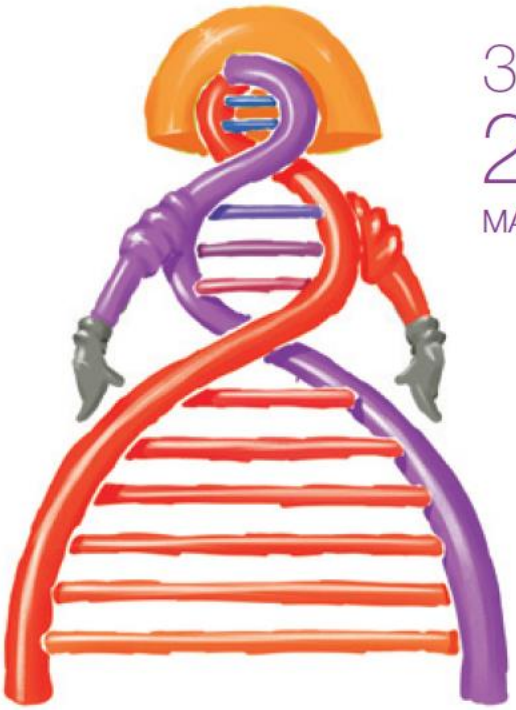

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ABSTRACTS BOOK

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A second-generation of tryptophan-containing small molecules extremely potent against HIV and EV-A71 clinical isolates

Olaia MARTÍ-MARÍ[1], Belén MARTÍNEZ-GUALDA[1], Sofia DE LA PUENTE-SECADES[1], Ernesto QUESADA[1], Liang SUN[2], Leen DELANG[2], Carmen MIRABELLI[2], Sam NOPPEN[2], Dominique SCHOLS[2], Johan NEYTS[2], Federico GAGO[3], María-José CAMARASA[1], Ana SAN-FÉLIX[1]

[1] Instituto de Química Médica (IQM-CSIC), Madrid, Spain.

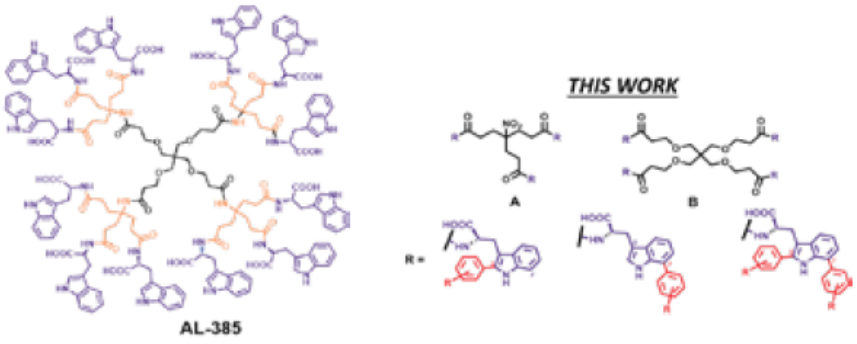
[2] Department of Microbiology and Immunology, Rega Institute for Medical Research, Leuven, Belgium.

[3] Department of Biomedical Sciences, Universidad de Alcalá, Alcalá de Henares, Madrid, Spain.

Contact e-mail: anarosa@iqm.csic.es

We have recently reported a family of tryptophan (Trp) dendrimers that are dual inhibitors of HIV and EV-A71.[1,2] The prototype compound (**AL-385**, MW: 3575.84 Da) is a tetrapodal derivative with a pentaerythritol core, 4 trivalent spacer arms and 12 tryptophan (Trp) units on the periphery. These Trp moieties are linked to the central scaffold through their amino groups, consequently their carboxylic acids are free and exposed to the surface.

In the present study, a scaffold simplification strategy was applied to reduce the structure complexity and molecular weight of the prototype. With this aim, tri- (**A**) or tetrapodal (**B**) Trp derivatives bearing differently substituted phenyl rings at C2 or/and C7 positions of the indole ring were prepared. The synthesis of these compounds implies the formation of new C-C bonds through metal-catalyzed (Pd II) cross-coupling reactions.[3] Biological results demonstrated that the novel half-sized Trp derivatives (1500 Da versus 3575.84 Da) are considerably more active against HIV-1/HIV-2 (10 to 100-fold times) and EV71 (8-fold times) than the prototype while having little or no adverse effects on the host cells (at concentrations up to 100 μM). As demonstrated earlier for the dendrimer prototype, these compounds inhibit early steps of the replicative cycle of HIV-1 and EV-A71 by interacting with their respective viral surfaces (glycoprotein gp120 of HIV and 5-fold vertex of the EV71 capsid).



References:

[1] Rivero-Buceta, E.; Doyagüez, E. G.; Colomer, I.; Quesada, E.; Mathys, L.; Noppen, S.; Liekens, S.; Camarasa, M-J.; Pérez-Pérez, M-J.; Balzarini. J.; San-Félix, A. *Eur. J. Med.Chem.* **2015**, 34-43.

[2] Rivero-Buceta, E.; Sun, L.; Martínez-Gualda, B.; Doyagüez, E. G.; Donkers, K.; Quesada, E.; Camarasa, M-J.; Delang, L.; San-Félix, A; Neyts, J.; Leyssen. P. *Antimicrob. Agents and Chemother,* **2016**, *60*, 5064-5067.

[3] Preciado, S.; Mendive-Tapia, L.; Albericio, F.; Lavilla, R. *J. Org. Chem.* **2013**, *78*, 8129-8135.