

Conferencias 2011



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PPH dendrimers, immune response and anti-inflammatory properties

Aula de Seminarios do CIQUS
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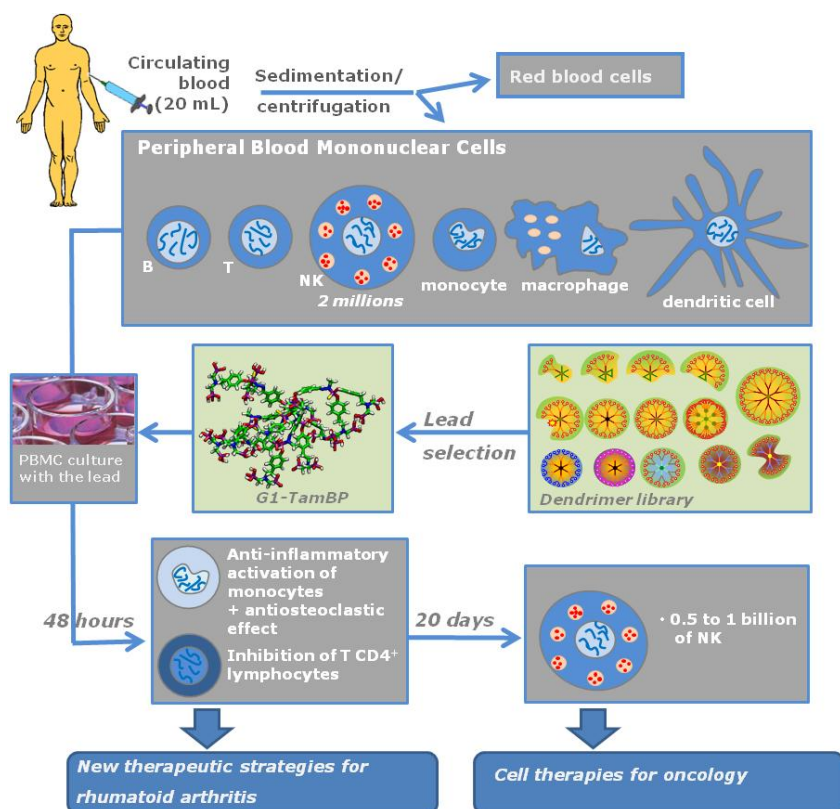
PPH dendrimers, immune response and anti-inflammatory properties.

Cédric-Olivier Turrin

We have recently shown that a series of poly(phosphorhydrazone) (PPH) dendrimers equipped with phosphonate end-groups can provoke ex-vivo an activation and/or an amplify some subsets of cells belonging to the human immune system, in collaboration with R. Poupot, J.J. Fournier and J.L. Davignon (INSERM U563, Toulouse Purpan, UPS Toulouse). This collaborative project led us to *i)* optimize the structure of the first hit, *ii)* explore the biological mechanism that may be related to these unprecedented properties.

The structural optimization of the first hit will be presented. A large dendrimer library has been obtained by a sequential modification of the structural parameters, ie surface function, size and generation, inner structure, outer-shell density.

The ex-vivo biological properties (Natural Killer cells amplification, anti-inflammatory activation of monocytes, effects on osteoclastogenesis) and the latest in-vivo results will also be briefly exposed. The use of fluorescent or biotine-functionalized analogs allowed us to uncover a part of the complex mechanisms involved in these processes. These insights will be related to possible therapeutic approaches.



- Phosphorus-based dendrimer as nanotherapeutics targeting both inflammation and osteoclastogenesis in experimental arthritis, *Sci. Transl. Med.* **3**, 81ra35 (2011)
- Efficient synthesis of phosphorus-containing dendrimers capped with isosteric functions of amino-bismethylene phosphonic acids, *Tetrahedron Lett.*, **50**, 2078-2082 (2009).
- Regulatory activity of azabisphosphonate-capped dendrimers on human CD4⁺ T cell proliferation for ex-vivo expansion of NK cells from PBMCs and immunotherapy, *J. Trans. Med.*, 7:82 (2009).
- *Bioorg. Med. Chem. Lett.*, **19**, 3963-3966 (2009).
- Anti-inflammatory and immunosuppressive activation of human monocytes by a bioactive dendrimer, *J. Leukocyte Biol.*, **85**, 553-562 (2009).
- Tailored control and optimisation of the number of phosphonic acid termini on phosphorus-containing dendrimers for the ex-vivo activation of human monocytes, *Chem. Eur. J.*, **14**, 4836-4850 (2008).
- Multiplication of human natural killer cells by nanosized phosphonate-capped dendrimers, *Angew. Chem. Int. Ed.*, **46**, 2523-2526 (2007).
- Design of phosphorylated dendritic architectures to promote human monocyte activation, *FASEB J.*, **20**, 2339-2351 (2006).
- See also: WO2005052032, WO2005052031, WO2006024769 & WO2010013086