

## Human $\gamma\delta$ T cell responses to infections and cancer: From basic immunology to immunotherapy

**Marc Bonneville**

Cancer Research Center Nantes-Angers, INSERM, IRT-UN, France

V $\gamma$ 9V $\delta$ 2 T lymphocytes are a major  $\gamma\delta$  T cell subset in adults that makes up 0.5 to 5 % of the peripheral lymphoid pool. V $\gamma$ 9V $\delta$ 2 T cells recognize a broad set of activated, transformed or infected cells in vitro. Accordingly they are expanded in vivo in a variety of infectious or tumor contexts. This broad reactivity pattern is primarily accounted for by recognition of small non-peptidic phosphorylated compounds, referred to as « phosphoantigens » (P-Ag), that correspond to metabolites of the isoprenoid biosynthetic pathway used by both mammalian cells and micro-organisms. How exactly P-Ag are sensed by V $\gamma$ 9V $\delta$ 2 T cells remains unknown. I will present recent unpublished result showing a unique and mandatory role played by a new member of the extended B7 receptor family in this activation process. From a more applied standpoint, the broad antimicrobial and antitumor reactivity of V $\gamma$ 9V $\delta$ 2 cells, their strong cytolytic and bactericidal activities, and their ability to produce inflammatory cytokines suggest a protective role played in infectious and tumor immunity. These observations, together with the recent availability of clinical grade compounds able to activate V $\gamma$ 9V $\delta$ 2 T cells in vitro and in vivo, have fostered development of immunotherapeutic strategies targeting this lymphoid subset in various clinical settings. I will review the latest results from immunotherapeutic trials in cancer and chronic infections, that rely on either adoptive transfer of in vitro expanded autologous V $\gamma$ 9V $\delta$ 2 T cells or in vivo treatment with clinical grade V $\gamma$ 9V $\delta$ 2 T cell agonists.

### Biography

Marc Bonneville has completed his postdoctoral studies from MIT (Cambridge, MA) in 1989, and has been heading since then a team working on human cellular immunity within a Cancer Research Center in Nantes (France). He co-founded in 1999 the biotech company Innate Pharma SA, which implements new immunotherapies targeting innate lymphocytes in infectious diseases and cancer. M.B. is author of more than 200 peer-reviewed papers (including Nature, Science, Cell, PNAS, Immunity,...) and 8 patents. He has received several awards (Bronze and Silver CNRS medal, Halpern and LNCC prizes), and has been involved in more than 30 scientific councils.

[marc.bonneville@nantes.inserm.fr](mailto:marc.bonneville@nantes.inserm.fr)