UPR 4301 Conventionnée
avec l'Université d'Orléans
et affiliée à l'Inserm

Docteur Jean-Claude BELŒIL
Directeur

SEMINAIRE EXTERNE
8 juillet 2011
SALLE DE CONFÉRENCES

Vendredi 8 juillet 2011 à 11 h 00

À l'invitation de Claudine Kieda

" Molecular and cellular mechanisms of cancer vaccines activity "

Professeur Andrzej Mackiewicz

Chair of Medical Biotechnology
Department of Cancer Immunology
University of Medical Sciences
Greater Poland Cancer Centre
15, Garbary Street
61866 Poznan Poland

Active specific and non-specific immunotherapy of cancer is in rapid development. First therapeutic cancer vaccine and immunostimulatory antibodies have been recently approved for cancer treatment. We have developed therapeutic gene modified allogeneic whole cell melanoma vaccine (AGI-101H) composed of two allogeneic melanoma cell lines Mich-1 (HLA-A1,A2), and Mich-2 (HLA-A3), stably transduced with designer molecular adjuvant Hyper-IL6 (H6), which express whole spectrum of melanoma antigens. H6 is a fusion protein comprising interleukin 6 (IL-6) and agonistic soluble IL-6 receptor.. AGI-101 vaccine primes at three different levels. First, H6 directly targets gp130 subunit of the IL-6 receptor complex. H6 acts in autocrine and paracrine manner. It auto activates Mich-1-H6 and Mich-2-H6 cells what alters the vaccine cells phenotype (secrete: IL-2, IL-8, IL-12, INFγ, GM-CSF, VEGF, RANTES). In the paracrine manner at the site of vaccination H6 inhibits formation of T regs, induces maturation of DCs and presentation of cryptic antigens, induces production of GM-CSF by T lymphocytes, activates NK cells, enhances formation of CD4+ and CD8+ memory cells and balances immune response towards Th1 type. HLA alloantigens provide next co-stimulatory signal, further enhanced by H6. Third, vaccine cells are coated with trace amounts of FBS, coming from the culture medium, which elicits cellular and antibody responses in immunized patients. In repeated vaccinations FBS specific CD4+ T cells may recognize FBS on DCs. CD154-CD40 interaction between FCS specific T cells and DC carrying FBS and tumor antigens may further augment anti-melanoma immune response.