P228. IMGT/mAb-DB: the IMGT® database for therapeutic monoclonal antibodies
Claire POIRON, Yan WU, Chantal GINESTOUX, François EHRENMANN, Patrick DUROUX and Marie-Paule LEFEVRE

IMGT®, the international ImMunoGeneTics information system®, Université Montpellier 2, Laboratoire d’immunogénétique Moléculaire LIGM, Institut de Génétique Humaine IGH, UPR CNRS 1142, Montpellier, France

IMGT/mAb-DB is the monoclonal antibodies database of IMGT®, the international ImMunoGeneTics information system® (http://www.imgt.org) that is the global reference in immunogenetics and immunoinformatics. IMGT/mAb-DB provides a unique expertised resource on immunoglobulins (IG) or monoclonal antibodies (mAb) developed for diagnostic or therapeutic purpose, and on fusion proteins for immune applications (FPIA). The IMGT/mAb-DB Query page allows requests on: (i) IMGT/mAb-DB ID, International Nonproprietary Name (INN) and number from the World Health Organization (WHO) INN Programme, INN proposed and recommended list, common and proprietary name (for instance, query can be made on IMGT/mAb-DB ID: 156, Infliximab, 7602, L77 (1997), R39 (1998), CA2 or REMICADE®), (ii) receptor type (IG or FPIA), the origin species (murine, rat, human, chimeric, humanized), Isotype or fusion protein format (IG and FPIA, respectively), radiolabelled and/or conjugated forms, IMGT/mAb-DB entries with links to IMGT/2Dstructure-DB (protein sequences) and IMGT/3Dstructure-DB (three-dimensional structures), (iii) specificity including target (antigen, ligand) and its origin (clone species and clone name), (iv) pharmaceutical company, clinical indication and development status, organization that approved the drug such as Food and Drugs Administration (FDA), European Medicines Agency (EMA) (for instance, query can be made on Rheumatoid arthritis [RA], Phase M, FDA or 1999), and (v) application (diagnostic and/or therapeutic) and clinical domain. IMGT/mAb-DB entries correspond to about two hundred clinical indications covering ten clinical domains with essentially oncology and immunology. There is a choice of twenty-six fields that the user can select for the results display. By providing links to IMGT/2Dstructure-DB (amino acid sequences and IMGT Collors do Perles) and IMGT/3Dstructure-DB (3D structures) for entries available in these databases, IMGT/mAb-DB facilitates comparative studies of antigen receptors and FPIA, and of their constitutive chains, even if 3D structures are not yet available. Since 2008, amino acid sequences of mAb (suffix -mab) and of FPIA (suffix -cepl) from the WHO/INN Programme have been entered in IMGT®. In June 2010, IMGT/mAb-DB contains 343 entries (175 -mab, 15 -cepl). 213 have an INN and, among them, 81 have sequences in IMGT/2Dstructure-DB. IMGT/mAb-DB is upgraded regularly. IMGT/mAb-DB is freely available for academics at http://www.imgt.org.

P229. IMMUNE TOLERANCE TO FULLY MISMATCHED ALLOGRAFTS USING CD3 ANTIBODIES REQUIRES DELAYED TREATMENT AT THE TIME OF T CELL ACTIVATION BURST
Sylvaine VOU, Université Paris Descartes and Inserm U913, 75015 Paris, France

CD3 antibody-treatment induces long-standing remission of autoimmunity by restoring self-tolerance; a finding successfully transferred to the clinic in autoimmune diabetes. It was therefore puzzling that, in mice receiving organ allografts, treatment with CD3 antibodies induced immunosuppression but no permanent survival. Here we revisited this issue based on the experience in autoimmunity showing that CD3 antibody-induced tolerance was only observed in primed hosts. We report, using a fully mismatched islet allograft model that CD3 antibody treatment led to significant yet limited survival if treatment was started at the time of transplant (day -1). In sharp contrast, permanent graft acceptance was observed when treatment was delayed by day 7 post-transplant at the time of the allreactive T cell burst. Importantly, long-term survival (>100 days) of second islet grafts of the original but not third party donors proved for the induction of antigen-specific tolerance in mice having received the delayed CD3 antibody treatment. Mononuclear cell infiltrate was detected within long-term surviving grafts but was not invasive nor destructive and included significant numbers of CD4+Foxp3+ regulatory T cells. Splenic cells from recipients treated on day 7 post-transplant and showing permanent graft acceptance exhibited decreased anti-donor mixed lymphocyte culture and IFN-gamma ELISPOT responses contrasting with normal reactivity to third-party alloantigens and they also effectively transferred tolerance. In situ gene signatures of tolerated islet grafts evidenced a down-regulation of IFN-gamma over Foxp3 and over-expression of TOA1-1, a new marker of tolerance. In conclusion, our data support the notion that in the case of CD3 antibodies, one essential factor determining their ability to promote a long-standing antigen-specific tolerance, is compared to just an immunosuppressive effect, is the timing of administration which must intervene during the initial burst of antigen-specific T cell activation.