# ABSENCE OF C4d DEPOSITION IN HUMAN COMPOSITE TISSUE (HANDS AND FACE) ALLOGRAFT BIOPSIES: AN IMMUNOPEROXIDASE STUDY

**J. Kanitakis**,[1, 2] B. McGregor,[2] L. Badet,[3] P. Petruzzo,[3] E. Morelon,[4] B. Devauchelle[5] and J.M. Dubernard[3]

([1]Depts. of Dermatology, [2]Pathology, [3]Transplant Surgery and [4]Immunology & Renal Transplantation, Ed. Herriot Hospital, Lyon; [5]Dept. of Maxillofacial Surgery, Amiens University Hospital, Amiens, France)

**Background**: Deposition of the C4d complement degradation product is a recognized marker of antibody-mediated rejection of solid organ allografts, including kidney, heart, liver and lung.[1] Its presence is associated with a poorer allograft outcome.[2]

**Objectives**: To investigate whether C4d deposition would be useful to monitor rejection in human composite tissue allografts (CTA).

**Methods**: We studied retrospectively 23 skin biopsies taken from the forearms of three patients with double hand allografts (HHA) and 41 mucocutaneous biopsies taken from the buccal mucosa, a sentinel skin graft and the facial skin of the first patient with a HFA. The biopsies, obtained from day 7 to year 7 postgraft, were formalin-fixed & paraffin-embedded (n:60) or snap-frozen in liquid nitrogen (n:4). They were classified according to a pathological score assessing CTA rejection,[3] and included 13, 30, 18 and 3 specimens with rejection scores 0, I, II and III, respectively. Paraffin-embedded and frozen biopsies were immunostained for C4d by an immunoperoxidase and an indirect immunofluorescence technique (IF), respectively. Paraffin-embedded kidney biopsies (shown to contain C4d deposits by IF on frozen sections) served as positive controls. The presence of anti-donor HLA class I/II alloantibodies was monitored with an ELISA technique on sequential blood samples (34 from the HHA patients and 14 from the HFA patient).

**Results**: Control kidney biopsies showed a characteristic deposition of C4d around peritubular capillaries. C4d deposition was not found in any of the specimens studied (either formalin-fixed or fresh frozen), even in those with the highest rejection scores. No HLA alloantibodies were detected in any of the patients during the study period.

**Conclusion**: These results suggest that humoral rejection occurs very rarely, if at all, in human CTA. They are at variance with a previous study on cynomolgus monkeys showing the presence of anti-donor antibodies and C4d deposition in hand allografts,[4] and further highlight differences that may exist between animal models and humans. Further studies are warranted in order to better assess which role, if any, humoral rejection mechanisms possibly play in human CTA.

**References**

1. Nickeleit V et al. *J Am Soc Nephrol* 2002;13:242.
2. Regele H et al. *Nephrol Dial Transpl* 2001;16:2058.
3. Kanitakis J et al. *Eur J Dermatol* 2005;15;235.
4. Cendales L et al. *Transplantation* 2005;80:1447.