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Transplantation of human stem cells from the umbilical cord to prevent or repair perinatal brain injury: A pre-clinical study

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Cerebral palsy is a disorder affecting the perinatal developing brain and causing motor and cognitive deficits. There is no treatment to date. Cell therapy is promising. The human umbilical cord (hUC) contains many stem cell types with important advantages including few ethical issues. Our goal is to investigate the potential of hUC blood mononuclear cells (hUCB-MNCs) or mesenchymal stem cells from the hUC Wharton's jelly (hUC-MSCs) to prevent or repair brain lesions in a rat model of neonatal brain injury. To inject cells, we used various routes of administration (intraperitoneal (i.p.), intracranial (i.c.) or intravenous (i.v.)), cell amounts (10^6, 10^7) and delays after injury. Cell fate and effects of transplantation on brain lesions were studied using molecular biology and histological techniques. We showed that i.p. injected hUCB-MNCs could not enter the systemic circulation. However, the injection of 10^7 hUCB-MNCs entailed a deleterious increase exclusively in the white matter (WM) lesion size, with perilesional microgliosis and the increase in serum concentrations of several cytokines. Contrarily, the i.p. injection of 10^6 hUCB-MNCs decreased the cortical lesion size. hUCB-MNCs injected i.v., soon or 24 hours after injury, had no effect at any concentration used. First i.c. injections of hUC-MSCs attenuated astrogliosis in the perilesional WM. To conclude, in most conditions tested, hUCB-MNCs could not integrate into the developing brain or promote repair. The i.p. injection of high amounts of hUCB-MNCs aggravated WM damage with systemic inflammation, while small amounts decreased the cortical lesion size. Preliminary results with hUC-MSCs support their possible protective role

Biography

Jérémie Dalous has completed his Ph.D in cell biology and biophysics from the Joseph Fourier University in Grenoble (France) and collaborated with the Max-Planck Institute of Biochemistry in Munich (Germany). He then got a first postdoctoral position from Göttingen University School of Medicine (Germany). He is now working in Paris (France) in the laboratory UMR676-INSERM-Paris Diderot University, where he develops innovative cell therapy strategies to prevent or repair neonatal brain lesions with stem cells from the human umbilical cord.

He has published 14 papers in peer-reviewed journals and is serving as a reviewer for international journals. He was awarded from several organizations (French Research Ministry, French Association for Research on Cancer, EMBO (European Molecular Biology Organization), the PremUp Foundation)

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