JCB article: The epithelial–mesenchymal transition: new insights in signaling, development, and disease

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Abstract
The conversion of an epithelial cell to a mesenchymal cell is critical to metazoan embryogenesis and a defining structural feature of organ development. Current interest in this process, which is described as an epithelial–mesenchymal transition (EMT), stems from its developmental importance and its involvement in several adult pathologies. Interest and research in EMT are currently at a high level, as seen by the attendance at the recent EMT meeting in Vancouver, Canada (October 1–3, 2005). The meeting, which was hosted by The EMT International Association, was the second international EMT meeting, the first being held in Port Douglas, Queensland, Australia in October 2003. The EMT International Association was formed in 2002 to provide an international body for those interested in EMT and the reverse process, mesenchymal–epithelial transition, and, most importantly, to bring together those working on EMT in development, cancer, fibrosis, and pathology. These themes continued during the recent meeting in Vancouver.

Discussion at the Vancouver meeting spanned several areas of research, including signaling pathway activation of EMT and the transcription factors and gene targets involved. Also covered in detail was the basic cell biology of EMT and its role in cancer and fibrosis, as well as the identification of new markers to facilitate the observation of EMT in vivo. This is particularly important because the potential contribution of EMT during neoplasia is the subject of vigorous scientific debate (Tarin, D., E.W. Thompson, and D.F. Newgreen. 2005. Cancer Res. 65:5996–6000; Thompson, E.W., D.F. Newgreen, and D. Tarin. 2005. Cancer Res. 65:5991–5995).

Abbreviations used in this paper: BMP7, bone-morphogenic protein 7; EGFR, EGF receptor; EMT, epithelial–mesenchymal transition; ER, estrogen receptor; FSP1, fibroblast-specific protein 1; GSK, glycogen synthase kinase; ILK, integrin-linked kinase; MET, mesenchymal–epithelial transition; MMP, matrix metalloproteinase; OSE, ovarian surface epithelium; PARP-1, poly-ADP-ribose polymerase 1; ROS, reactive oxygen species; siRNA, small interfering RNA

REVIEW INAUGURAL BODEN EMT CONFERENCE, PORT DOUGLAS QLD, AUSTRALIA, 2003

The Boden Conference on Epithelial-Mesenchymal Transitions (EMT) was held on October 5th-8th 2003 at Port Douglas, Queensland. The meeting was convened locally by Don Newgreen (Murdoch Childrens Research Inst.), Erik Thompson (Bernard O'Brien Inst. of Microsurgery) and Guy Lyons (Sydney Cancer Centre) with a powerful international committee chaired by Professor Elizabeth Hay (Harvard Medical School, Boston, USA) and including US, Canadian, Japanese, German and French members. The principal supporter of the conference was the Boden Foundation. The Potter Foundation provided Keynote speaker support, the Australian Association of Science, and a number of Australian research institutes provided essential support. Major international support was provided by the NIH (USA).

EMT is the name given to a very complex set of changes in cell behaviour, involving differential expression of many genes and alterations in function of many cellular and extracellular molecules. The outcome of this is the transformation of cells arranged in a coherent layer—epithelial cells-- to more individualistic and potential motile cells—mesenchymal cells. EMT was recognised decades ago (by Prof. Hay) as a primary mechanism in embryogenesis for remodelling tissues. More recently EMT has been seen as crucial to the spread and invasion of carcinoma, and more recently still, various pathologies marked by fibrosis have had their resemblances to EMT explored. Despite the basic and clinical importance of EMT, this extremely rapidly growing field has never had a conference devoted to it, and indeed the disciplines of developmental biology, cancer and pathology rarely interact although they have much to share.

This Conference addressed these shortcomings by bringing together 120 international and Australian experts spanning each of these disciplines. Outstanding Keynote lectures were given by Professors Elizabeth Hay, Mary Hendrix (University of Iowa, USA) and Jean Paul Thiery (Inst. Curie, Paris, France). The quality and standing of the speakers in the general sessions was also remarkably high, with thirty-seven of forty-six speakers international. This international attractiveness is a tribute to the timeliness of the meeting. Given the common interests, the sessions were intense and replete with new data, and the discussions were full and lively.

The same molecular families were repeatedly identified in examples from development, cancer and pathology, highlighting the similarity (but not identity) of EMTs in different biological contexts, both normal and pathological. These included the intercellular growth factor signals especially of the TGF-beta and Wnt families; their receptors on the cell surface and, within the cells, the signal transduction chains, Smads and beta-catenin. These exerted control of EMT by regulating expression of so-called master genes, whose protein products regulate and orchestrate transcription of other genes. Most attention was focussed on the Slug/Snail family which collaborate with the LEF/TCF gene family to control the expression of genes for EMT effector molecules. The coordinated functions of the numerous effector molecules was one of the recurrent themes, with particular attention on the cadherin system of cell-cell adhesion, and the cytoskeleton and its regulators of the Rac/Rho family. Taken together the talks emphasised the

complex nature of the changes in EMT and hence the exquisite orchestration required to carry it out.

The basic science of EMT also highlighted key points where the process might be controlled clinically; and indeed there were exciting reports on the ability to halt and even reverse EMT in models of renal fibrosis. The medical implications of this are enormous, given the prevalence of fibrosis contributory to, for example, renal failure in human disease.

EMT is a dynamic process, and many of the talks, including that of Prof. Thiery, included spectacular state of the art time-lapse imaging. As well as being visually stunning, these gave insights into cellular processes which are otherwise difficult to comprehend.

This Boden Conference amply fulfilled its aims of bringing together in a cross-disciplinary forum, the worlds leading experts on a topic of enormous basic and clinical interest that is currently in a phase of rapid growth. As an indicator of the success of this conference, plans for future EMT Conferences were unanimously agreed upon during one of the open discussion sessions. These are planned for Vancouver, Canada, in the Northern Autumn of 2005 (Organizers: Shoukat Dedhar and Raghu Kalluri) and Montpellier, France, in 2007 (Organizer: Pierre Savagner).