Research Programmes

Oncology

Eduard Batlle: Colorectal cancer laboratory

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Highlights

- Normal intestinal stem cells (ISCs) continuously repopulate the epithelium. ISCs are marked by high expression of the EphB2 receptor, which becomes gradually silenced as cells differentiate. Using EphB2, we have purified and profiled ISCs, crypt proliferative progenitors and late transient amplifying cells from mice and human intestine. Moreover, for the first time we have established robust *in vitro* culturing conditions for human colon stem cells.
- A frequent complication in colorectal cancer (CRC) is regeneration of the tumor upon therapy. We have shown that CRC relapse is associated with the presence of ISC-like cells in aggressive tumors.
- The formation and maintenance of complex organs requires segregation of distinct cell populations into defined territories (*i.e.* cell sorting) and the establishment of boundaries between them. EphB/ephrin-B signaling is crucial for the correct compartmentalization of epithelial cells in the intestinal mucosa. EphB receptors interact with E-cadherin and with the metalloproteinase ADAM10 at sites of adhesion and their activation induces shedding of E-cadherin by ADAM10 at interfaces with ephrin-B1 expressing cells. This process results in asymmetric localization of E-cadherin and, as a consequence, in differences in cell affinity between EphB+ and ephrin-B+ cells.

Publications

- Casagolda D, Del Valle-Pérez B, Valls G, Lugilde E, Vinyoles M, Casado-Vela J, Solanas G, Batlle E, Reynolds AB, Casal JI, de Herreros AG and Duñach M. A p120-catenin-CK1epsilon complex regulates Wnt signaling. J Cell Sci, 123 (Pt 15), 2621-31 (2010)

Collaborations

- A role for TGB-beta in CRC progression. Elena Sancho, IRB Barcelona (Barcelona, Spain)
- Antibodies against Intestinal Stem Cell genes involved in CRC. Francesc Mitjans, Leitat (Barcelona, Spain)
- Common genes in pancreas cancer and CRC. Francisco X Real, Spanish National Cancer Research Center (Madrid, Spain)
- Control of intestinal stem cell positioning. Hans Clevers, Hubrech Laboratory (Utrecht, Netherlands)
- Development of metastatic models of CRC. Ramon Mangues, Hospital de la Santa Creu i Sant Pau (Barcelona, Spain); Maria Virtudes Céspedes, Hospital de la Santa Creu i Sant Pau (Barcelona, Spain)
- *Drosophila* gut as a model for CRC development. Andreu Casali, IRB Barcelona (Barcelona, Spain)
- Eph signalling in pancreas development. Francisco X Real, Spanish National Cancer Research Center (CNIO) (Madrid, Spain)
- Intestinal stem cells in CRC. Hans Clevers, Hubrecht Laboratory (Utrecht, Netherlands)
- Isolation of colorectal cancer stem cells using Wnt target genes. Gabriel Capellà, Institut Català d'Oncologia (Hospitalet de Llobregat, Spain)

- Mediators of EMT in *Drosophila* and CRC. Jordi Casanova, IRB Barcelona (Barcelona, Spain)
- Mediators of EMT in CRC. Mireia Duñach, Autonomous University Barcelona (Cerdanyola del Vallés, Spain); Antonio García de Herreros, Institut d'Investigació Mèdica (IMIM) (Barcelona, Spain)
- Regulation of Wnt signaling in CRC. Giancarlo Marra, Institute of Molecular Cancer Research (Zurich, Switzerland)
- Regulation of Wnt signalling pathway in CRC. Mireia Duñach, Autonomous University of Barcelona (Barcelona, Spain); Antonio García de Herreros, IMIM (Barcelona, Spain)
- Role of cdk6 in intestinal development. Mariano Barbacid and Marcos Malumbres, Spanish National Cancer Research Center (Madrid, Spain); Esther Stoeckl, University of Zurich (Zurich, Switzerland)
- Stem cell gene expression signatures in the prediction of CRC outcome. José Baselga, Vall d'Hebrón Hospital (Barcelona, Spain)
- Telomerase length in intestinal Stem Cells. Maria A. Blasco, Spanish National Cancer Research Center (CNIO) (Madrid, Spain)
- TGF-beta signaling in Inflammatory Bowel Disease. Azucena Salas, Institut d'Investigacions Biomèdicas August Pi i Sunyer (Barcelona, Spain)
- TGF-beta target genes in CRC. Joan Massagué, Memorial Sloan-Kettering Cancer Center (New York, United States)
- The genetic programmes linked to EphB down-regulation during CRC progression. Giancarlo Marra, Institute of Molecular Cancer Research, University of Zurich (Zurich, Switzerland)

Research projects

- Biología del cáncer (ONCOBIO). Consolider Ingenio-2010 (CSD2007-00017). Spanish Ministry of Science and Innovation (MICINN). 2007-2012. Principal investigator: Eduard Batlle
- Caracterizacion de genes estromales promotores de la progresion y la diseminacion metastasica en el cancer colorectal. Proyectos de investigación fundamental (SAF2009-11757). Spanish Ministry of Science and Innovation (MICINN). 2010. Principal investigator: Elena Sancho
- Convenio de colaboración entre la Fundación Científica de la Asociación Española contra el Cáncer y la Fundación Privada Institut de Recerca Biomèdica en materia de ayudas para investigadores en el ámbito de la oncología, Fundación AECC Investigación del Cancer, (2009-2010). Principal investigator: Eduard Batlle
- Dissecting the roles of the beta-catenin and Tcf genetic programmes during colorectal cancer progression, European Commission, ERC-2007STG-208488, (2008-2012). Principal investigator: Eduard Batlle
- Laboratory de cancer colorrectal i biologia del epiteli intestinal. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 989). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Eduard Batlle
- Señalización por Wnt, receptores Eph y cáncer de colon: un análisis funcional del inicio de la tumorigénesis intestinal. Proyectos de investigación fundamental (SAF2008-01512). Spanish Ministry of Science and Innovation (MICINN). Principal investigator: Eduard Batlle
- Êcole Polytechnique Fédérale de Lausanne, EPFL-DLSA, (2006-open). Principal investigator: Eduard Batlle

Awards and honours

- Premi Banc de Sabadell a la Investigació Biomèdica. Fundació Banc Sabadell (2010). Awardee: Eduard Batlle

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