Research Programmes

ONCOLOGY

Eduard Batlle: Colorectal Cancer

Group Members

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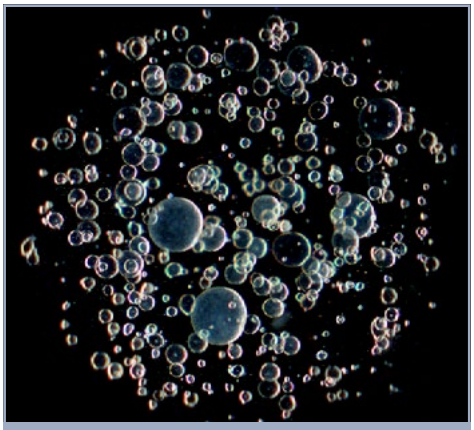
Highlights

- Normal intestinal stem cells (ISCs) continuously repopulate the epithelium. We have purified and profiled ISCs, crypt proliferative progenitors and late transient amplifying cells from mouse and human intestine. These data have paved the way to unequivocally identify ISC-like tumour cells in colorectal cancer (CRC) samples.
- A frequent complication in CRC is the regeneration of the tumour upon therapy. We have shown that CRC relapse is associated with the presence of ISC-like cells in aggressive tumours.
- For the first time we have established robust *in vitro* culturing conditions for human colon stem cells. This is an important development for adult stem cell research that may allow their use for regenerative medicine.
- The formation and maintenance of complex organs requires the segregation of distinct cell populations into defined territories and the establishment of cell boundaries. EphB receptors interact with E-cadherin and with ADAM10 metalloproteinase at adhesion sites and their activation induces shedding of E-cadherin by ADAM10 at interfaces with ephrin-B1-expressing cells. This results in asymmetric localization of E-cadherin and thus in differences in cell affinity between EphB+ and ephrin-B+ cells.



3D organoids derived from human colon intestinal stem cells expanded in vitro

Publications

- Campbell K, Whissell G, Franch-Marro X, Batlle E and Casanova J
  Specific GATA factors act as conserved inducers of an endodermal-EMT
  Dev Cell, 21, 1051-61 (2011)
- Janich P, Pascual G, Merlos-Suárez A, Batlle E, Ripperger J, Albrecht U, Cheng HY, Obrietan K, Di Croce L and Benitah SA.
  The circadian molecular clock creates epidermal stem cell heterogeneity
  Nature, 480, 209-14 (2011)
- Jung P, Sato T, Merlos-Suárez A, Barriga FM, Iglesias M, Rossell D, Auer H, Gallardo M, Blasco MA, Sancho E, Clevers H and Batlle E.
  Isolation and in vitro expansion of human colonic stem cells
  Nat Med, **17**, 1225-7 (2011)
- Solanas G, Cortina C, Sevillano M and Batlle E.
  Cleavage of E-cadherin by ADAM10 mediates epithelial cell sorting downstream of EphB signalling
  Nat Cell Biol, **13**, 1100-7 (2011)
- Merlos-Suárez A, Barriga FM, Jung P, Iglesias M, Céspedes MV, Rossell D, Sevillano M, Hernando-Momblona X, da Silva-Diz V, Muñoz P, Clevers H, Sancho E, Mangues R and Batlle E.
  The intestinal stem cell signature identifies colorectal cancer stem cells and predicts disease relapse
  Cell Stem Cell, **8**, 511-24 (2011)
- Solanas G and Batlle E.
  Control of cell adhesion and compartmentalization in the intestinal epithelium
  Exp Cell Res, **317**, 2695-701 (2011)

PhD Theses

- *Molecular mechanisms involved in the initiation and progression of colorectal cancer*. Elisa Espinet Hernández, University of Barcelona (2011). Thesis director: Helena Sancho, Eduard Batlle. Honors: Summa Cum Laude

Other

- Member of the Scientific Advisory Committee for the Association for International Cancer Research (AICR)
- Member of the jury for the 2011 Banc de Sabadell Award

Research projects

- Biología del cáncer (ONCOBIO). Consolider Ingenio-2010 (CSD2007-00017). Spanish Ministry of Science and Innovation (MICINN). 2007-2012. 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
- Laboratori 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). 2009-2011. Principal investigator: Eduard Batlle
- Êcole Polytechnique Fédérale de Lausanne, EPFL-DLSA, (2006-open). Principal investigator: Eduard Batlle

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 and Eph signalling in pancreas development*. Francisco X Real, Spanish National Cancer Research Center (CNIO)(Madrid, Spain)
- *Development of metastatic models of CRC*. Ramon Mangues and 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)
- *Intestinal stem cells in CRC*. Hans Clevers, Hubrecht Laboratory (Utrecht, Netherlands)
- *Mediators of EMT in Drosophila and CRC*. Jordi Casanova, IRB Barcelona (Barcelona, Spain)

- *Role of cdk6 in intestinal development*. Mariano Barbacid and Marcos Malumbres, Spanish National Cancer Research Center (CNIO) (Madrid, Spain); Esther Stoeckl, University of Zurich (Zurich, Switzerland)
- *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 (IDIBAPS) (Barcelona, Spain)
- *TGF-beta target genes in CRC*. Joan Massagué, Memorial Sloan-Kettering Cancer Center (New York, United States)
- *The circadian molecular clock and stem cell niches*. Salvador Aznar-Benitah. Center for Genomic Regulation (CRG) (Barcelona, Spain)
- *Control of intestinal stem cell positioning,* Hans Clevers, Hubretch Laboratorium (Utrecht, Netherlands)
- *Stem cell gene expression signatures in the prediction of CRC outcome*. José Baselga, Vall d'Hebrón Hospital (Barcelona, Spain)

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