

CURRICULUM VITAE

Name: Eduard Batlle

Birth Date: 24th July 1970

Nationality: Spanish

Current Position: Chairman, Cancer Science Program, IRB Barcelona.
Group leader, Cancer Science Program, IRB Barcelona.
ICREA Research Professor.

Date of Start: 01/03/2004

URL for Website: www.irbbarcelona.org/en/research/colorectal-cancer-laboratory

Google scholar: <https://scholar.google.com/citations?user=uLX3exUAAAAJ&hl=en&oi=ao>

Researcher identifiers: ORCID: 0000-0003-2422-0326, Research ID: K-8080-2014

Education & Training:

- 2000-2003 Postdoctoral Fellow. Prof. Hans Clevers Lab. Hubrecht Laboratorium, Utrecht, Netherlands.
- 1999-2000 Postdoctoral Fellow. Prof. Miguel Beato's Lab. IMT. Marburg, Germany.
- 1995/1999 PhD in Biology. University of Barcelona (UB), Spain. Prof. Antonio García de Herrero's Lab. Institut Municipal d'Investigació Mèdica (IMIM), Barcelona, Spain.
- 07/06/1993 BSc in Biological Sciences. University of Barcelona (UB), Spain

AWARDS AND DISTINCTIONS

- 2021 King Jaume-I Award in Medical Research
- 2019 City of Barcelona Award in Life Sciences
- 2018 Medal from the International Foundation Olof Palme
- 2017 Francisco Cobos Foundation Award to Biomedical Research
- 2016 Carmen y Severo Foundation Ochoa Award
- 2016 Lilly Foundation Award in Pre-clinical studies
- 2015 Life Sciences National Award from Caja Rural de Granada Foundation
- 2014 The Pezcoller foundation-EACR Cancer Researcher Award
- 2013 Joseph Steiner Cancer Research Award (Berna, Switzerland)
- 2013 National Award in Cancer Research "Doctores Diz-Pintado"
- 2010 Banc de Sabadell Award for Research in Biomedicine
- 2006 Debiopharm Life Sciences Award (Lausanne, Switzerland)

European Research Council grants

- 2018 ERC Advanced Grant (ERC-AdvG)
- 2013 ERC Advanced Grant (ERC-AdvG)
- 2007 ERC Starting Grant (ERC-StG)
- 2018, 2014 ERC Proof of Concept Grant (ERC-PoC)

SELECTED PUBLICATIONS AS CORRESPONDING AUTHOR (2011-2021 period)

1. HERPERS B, et al. (27 AUTHORS) and **BATLLE E***, THROSBY M*. (shared corresponding authorship). Functional screening on patient-derived organoids identifies a therapeutic bispecific antibody that triggers EGFR degradation in LGR5⁺ tumor cells. **Nature Cancer** (accepted in principle).
2. TAURIELLO DVF, SANCHO E, and **BATLLE E**. Overcoming TGF β -mediated immune evasion in cancer. **Nature Reviews Cancer**. 2021. E-pub Oct 20. [Impact Factor: 60,72]

3. MORRAL C, et al., and **BATLLE E.** *Zonation of ribosomal DNA transcription defines a stem cell hierarchy in colorectal cancer.* **Cell Stem Cell**. 26: 845-861. 2020. [Impact Factor: 24,6; citations: 25]

→ This work has received **2** News & Views/Editorial Highlights

4. **BATLLE E** and MASSAGUE J. *Transforming Growth Factor- β Signaling in Immunity and Cancer.* **Immunity**. 50:924-940. 2019. [Impact Factor: 19,7; Citations: 629].

5. TAURIELLO DVF, et al. (16 AUTHORS) and **BATLLE E.** *TGF β drives immune evasion in genetically reconstituted colon cancer metastasis.* **Nature**. 554:538-543. 2018. [Impact Factor: 43,77; Citations: 889]

→ This work received **10** News & Views/Editorial Highlights: Science Signaling; Nat Rev Gastroenterol Hepatol, Nat Rev Clin Oncol, Nat Rev Cancer, Nat Rev Immunol, Trends in Cancer ([10.1016/j.trecan.2018.03.005](https://doi.org/10.1016/j.trecan.2018.03.005)), Trends in Immunology, Immunity (doi.org/10.1016/j.immuni.2018.03.037), British Journal of Cancer (doi.org/10.1038/s41416-018-0122-x), and Cancer Discovery. *It is amongst the top 1% most cited articles of similar age in all journals*

6. **BATLLE E** & CLEVERS H. Cancer stem cells revisited. **Nature Medicine**. 23 (10), 1124-1134. 2017. [Impact Factor: 32,6; Citations: 1294]

7. BARRIGA F, et al. (14 AUTHORS) and **BATLLE E.** *Mex3a marks a slowly dividing subpopulation of Lgr5+ Intestinal Stem Cells.* **Cell Stem Cell**. 20 (6): 801-816. 2017. [Impact Factor: 25,3; Citations: 114]

8. CORTINA C, et al. (9 AUTHORS) & **BATLLE E.** *A genome editing approach to study cancer stem cells in human tumors.* **EMBO Molecular Medicine**. 9 (7): 869-879. 2017. [Impact Factor: 10,2; Citations: 83]

→ News & Views in EMBO Mol Med ([doi: 10.15252/emmm.201707858](https://doi.org/10.15252/emmm.201707858))

9. CALON A, et al. (17 AUTHORS) and **BATLLE E.** *Stromal gene expression defines poor-prognosis subtypes in CRC.* **Nature Genetics** 47: 320-362. 2015. [Impact Factor: 35,2; Citations: 778]

→ This work received **6** News & Views/Editorial Highlights: Nature Genetics, EMBO Molecular Medicine, Cancer Discovery, Nat Rev Clin Oncol, Nat Rev Cancer, Nat Rev Gastroenterol Hepatol.

10. WHISSELL G, et al. (16 AUTHORS) and **BATLLE E.** *The transcription factor GATA6 enables self-renewal of colon adenoma stem cells by repressing BMP gene expression.* **Nature Cell Biology**. 16: 695-707. 2014. [Impact Factor: 20,7; Citations: 115]

→ Cover page, News & Views in EMBO J and Cancer Discovery

11. CALON A, et al. (15 AUTHORS) and **BATLLE E.** *Dependency of Colorectal Cancer on a TGF-Beta-Driven Program in Stromal Cells for Metastasis Initiation.* **Cancer Cell**. 22: 571–584. 2012. [Impact Factor: 24,7; Citations: 845]

→ Cover Page. Selected amongst the top 10 most influential articles published in **Cancer Cell** during 2012. “News & Views” by EMBO J and by Cancer Discovery.

12. JUNG P, et al. (10 AUTHORS) and **BATLLE E.** *Isolation and in vitro expansion of human colonic stem cells.* **Nature Medicine**. 17: 1125-1127. 2011. [Impact Factor: 24,3; Citations: 606]

13. SOLANAS G, CORTINA C, SEVILLANO M and **BATLLE E**. *Cleavage of E-cadherin by ADAM10 mediates epithelial cell sorting downstream of EphB signaling*. **Nature Cell Biology**. 13: 1100-1107. **2011**. [Impact Factor: 20.7; Citations: 168]
14. MERLOS-SUÁREZ A, et al. (12 AUTHORS) and **BATLLE E**. *The intestinal stem cell signature identifies colorectal cancer stem cells and predicts disease relapse*. **Cell Stem Cell**. 8(5): 511-524. **2011**. [Impact Factor: 25.3; Citations: 873]

INVITED PRESENTATIONS (selection of more than 100 invited talks in the past 5 years)

Oct 2021	Cold Spring Harbor Biology of Cancer: "Microenvironment & Metastasis" (virtual).
Apr 2021	American Association for Cancer Research (AACR) Annual Meeting (virtual).
Oct 2020	European Society of Molecular Oncology (ESMO) Congress (virtual).
Oct 2020	EORTC-NCI-AACR Symposium on Cancer Therapeutics (virtual).
Nov 2019	Cell Symposia: Hallmarks of Cancer. Seattle. US.
Nov 2019	EACR Conference "Goodbye Flat Biology: Advancing 3D-based Models for Cancer Biology and Drug Discovery". Berlin. Germany.
Oct 2019	2nd joint EACR-MRS Conference on "Seed and Soil". Berlin. Germany.
Sep 2019	Cell Plasticity in Colorectal Carcinogenesis Symposium. Frankfurt. Germany.
Sep 2019	Oxford Stem Cell Institute Symposium 2019. UK
May 2019	International Society Stem Cell Research (ISSCR) Annual Meeting; Los Angeles.
May 2019	EMBO Workshop on "Mesenchymal cells in inflammation, immunity and cancer", Athens.
Mar 2019	American Association for Cancer Research, AACR 2019 Annual Meeting. Atlanta. US.
Sep 2018	AACR meeting Intestinal Stem Cells and Colon Cancer: Biology to Therapy. Washington. US.
Sep 2018	EMBO Workshop on Cellular signaling and cancer therapy. Cavtat. Croacia.
Sep 2018	ISREC-SCCL Symposia "Horizon in Cancer Biology and Therapy". Lausanne. Switzerland.
Aug 2018	Metastasis Research Society Bi-annual meeting, Princeton University. US.
May 2018	Ho-am Forum on Medicine. Seoul. Korea.
Apr 2018	Speaker and session Chair. AACR Annual Meeting. Chicago. US.
Sep 2017	Victorian Comprehensive Cancer Center Inaugural symposium. Melbourne. AUS.
Jun 2017	Sigrid Jusélius Symposium. Helsinki. Finland.
Apr 2016	AACR Annual Meeting. New Orleans. US.
Apr 2016	EMBO EMBL Symposium: "Tumor microenvironment". Heidelberg. Germany

ORGANIZATION OF INTERNATIONAL CONFERENCES

2007,-12,-21	Organizer of Barcelona Biomed Conference: "Stem Cells and Cancer" (with Hans Clevers).
2018	Member of the organization committee for the 2019 International Society for Stem Cell Research (ISSCR) symposia on Stem Cells & Organoids in Development and Disease.
2015-2016	Member of the organization committee for 2017 ISSCR Annual Meeting.
2016	Co-organizer of the 2016 Barcelona Conference on Epigenetics and Cancer.
2009	Organizer of CNIO Cancer Conference: Stem Cells and Cancer (with Maria A. Blasco, Elaine Fuchs, and Mirna Pérez-Moreno).

MAIN RESEARCH PROJECTS GRANTED AS PI (selection of recent)

2020 – 2025: ERC Advanced Grant. ERC-2019-AdG 884623; ResidualCRC
 2020 – 2025: IMI network grant. EU/H2020. PERSIST-SEQ consortium.

2021 – 2023: Ministry of Science and Innovation. Proyectos I+D+i Retos.
2019 – 2024: CRUK /AECC. Accelerator Award: MACH3CANCER network.
2018 – 2023: CRUK/AECC. Accelerator Award: ACRCLerate network.
2019 – 2022: La Caixa Foundation Health Research 2018. HR18-00359.
2019 – 2021: World Wide Cancer Research. 19-0005.
2018 – 2021: Spanish Association for Cancer Research (AECC).
2014 – 2019: ERC Advanced Grant. ERC-2013-AdG 340176; EditCRC.
2013 – 2017: Josef Steiner Cancer Research Award.
2013 – 2016: FP7-HEALTH-2013- 601876 SUPPRESSTEM consortium:

Participation in International consortia

2020-2025: PERSIST-SEQ consortium. EU/H2020 funded. 6 academic partners (including Batlle lab), 4 small biotech companies and 3 large pharma companies (Astra-Zeneca, Bayer, Charles River). Focuses on identification of tumor cells that persist after therapy using single cell sequencing approaches.

<https://persist-seq.org/>

2018-2023: ACRCELerate: Colorectal Cancer Stratified Medicine Network. CR-UK/AECC/AICR funded. 10 groups in UK, 2 Italy and 3 Spain (including the Batlle lab). Focuses on development of new treatment paradigms for CRC.

<https://www.beatson.gla.ac.uk/ACRCelerate/teams.html> .

2019-2024: MACH3CANCER network. CR-UK/AECC funded. 11 groups in UK + Batlle Lab. Aims at developing new microscopy techniques to study 3D cancer models.

<https://mach3cancer.org/>

2013-2016: SUPPRESSTEM. Funded by EU (FP7 program). 3 partners in The Netherlands + 1 UK + Batlle lab. This consortium developed MCLA-158, a bi-specific antibody that targets cancer stem cells. It is currently being tested in phase-1 clinical trials (see below).

<https://cordis.europa.eu/project/id/601876/reporting>

INSTITUTIONAL RESPONSIBILITIES

2005-present Chairman of the Cancer Science Program at IRB Barcelona: Activities include designing the strategic lines of the programme, the identification and recruitment of new group leaders, mentoring junior programme members, writing institutional grants applications and organizing program activities.

2005-present Member of the direction committee of IRB Barcelona: This is the maximum decision-making organ regarding strategic and scientific issues in the institute.

SUPERVISION & MENTORING OF STUDENTS, POSTDOCTORAL FELLOWS AND JUNIOR PIs

9 students have obtained their PhDs with highest qualifications under my supervision, 2 of which are currently working for the pharmaceutical industry (G.Whissell & E.Montagni) and 5 are pursuing academic careers in renown centers (F.Barriga is a postdoc with Scott Lowe at MSKCC in NYC; Clara Morral with Andy Minn at UPENN, and Carme Cortina at IRB Barcelona, Jordi Badia at IMIM with Alex Calon). Elisa Espinet trained as a PhD under my supervision, performed a postdoc with Andreas Trumpp at Hi-Stem in Heidelberg and she is currently a principal investigator at Univ. of Barcelona. Another, M. Iglesias, is MD/PhD working at the department of pathology at Hospital del Mar (Barcelona).

5 former postdoctoral fellows trained in my lab are also now independent group leaders (Enza Lonardo at Univ. of Naples; Danielle Tauriello at Radboud Univ. NL; Alexandre Calon at IMIM, Barcelona; and Peter Jung at Julius-Maximilians-University, München).

As chair of the Cancer Science program at IRB Barcelona I have mentored three junior group leaders; Roger Gomis, Travis Stracker and Alejo Rodriguez-Fraticelli.

PhD students in the 2017-2021 period

- Clara Morral. 17/07/2017. Pompeu Fabra University. Morral C, et al., & Batlle E. *Cell Stem Cell*. 2020. 26:845-861. She is currently undertaken postdoctoral training with Andy Minn (UPENN. Philadelphia. US).
- Gemma Turon. 25/04/2019. UB. Cortina C*, Turon G* et al., & Batlle E. *EMBO Mol Med*. 2017. 9(7): 869-879 *Shared First Authorship
- Mar Iglesias. 30/09/2019. MD/PhD. Stromal Biomarkers for CRC. UAB. Dep. Surgery. Patent application PCT/EP2020/077272. She works at Dept. of Pathology at Hospital del Mar.
- Jordi Badia. 14/01/2020. UB. He is currently a postdoc in the group of Alex Calon (IMIM)
- Ongoing PhD Thesis: 5 PhD students (1 of them belongs to the PhD4MD student program).

REVIEWING ACTIVITIES

- 2017-present Member of the editorial advisory board of EMBO Molecular Medicine.
- 2013 / 2020 Member of the evaluating panel for ERC-Consolidator Grants.
- 2020 Evaluation panel of junior PIs for Francis Crick Institute (London. UK).
- 2018 / 2021 Member of selection committee of new group leaders at EMBL Barcelona.
- 2017 Member of the jury of the Fundación Lilly Award
- 2015 Member of the jury for the 2016 Pezcoller Foundation/AACR Award
- 2005-2012 External Advisor for group leader search and evaluation committees at the Center for Genomic Regulation (CRG-Barcelona)
- 2011- 2015 Member of the Scientific Advisory Committee for World Wide Cancer Research
- 2011-present Member of the Jury for the Banc Sabadell Award.
- 2004-present Peer-reviewer of research projects for the ERC, Spanish Agency of Evaluation (ANEP); Associazione Italiana per la Ricerca sul Cancro; Cancer research UK, MRC, Netherlands Organization for Health Research and Development (ZonMw TOP grants), KWF, WWCR; INSERM and more.

PATENTS & LICENSE AGREEMENTS.

- WO/2017/069628. Priority date: 23/10/2015. Holder Entity: Merus NV, KNAW, Ocello B.V, IRB Barcelona and ICREA. This patent protects bi-specific antibody MCLA158 which is currently in clinical trials for the treatment of CRC and other solid tumors (NCT03526835). We licensed IP to MERUS. See section below.
- WO/2020/1046448. Priority date: 22-11-2018. Holder Entities: IRB Barcelona, ICREA, Barcelona Univ. Protects Compound H, a small molecule inhibitor of TGF-beta signaling.
- WO/2014/072517. Priority Date: 12-11-2012. Holder Entities: IRB Barcelona and ICREA. PCT/EP2020/077270 and PCT/EP2020/077272. Holder entities: IRB Barcelona, ICREA and UPF Univ and IRB Barcelona, ICREA and IMIM, respectively. Priority Dates: 30-09-2019. This family of patents protects biomarkers to detect a TGF-beta active microenvironment, and predict likely response to TGF-beta inhibitors, and unlikely response to immune checkpoint blockade therapies.

MAIN TECH-TRANSFER ACTIVITIES.

- Generation of a bi-specific LGR5 x EGFR therapeutic antibody MCLA-158, in collaboration with the pharmaceutical company MERUS. A patent was granted: WO/2014/072517. MCLA-158 is currently in phase 1 clinical trials for multiple EGFR and LGR5 dependent tumors (see section below for details).

- Development of companion diagnostic tests for TGF- β inhibitory therapies. Part of this program was funded by the Mind the Gap program of the Botin Foundation. A family of patents protect the biomarkers discovered (WO/2014/072517, PCT/EP2020/077270 and PCT/EP2020/077272). We are currently collaborating with several institutions and companies to implement the use of this test to stratify patients in an upcoming clinical trial based on treating cancer with TGF- β inhibitors.

- mENVIRON program in collaboration with pharmaceutical company MERUS. It is aimed at generating bi-specific antibodies to target distinct cell types of the tumor microenvironment. Several lead candidates are currently on preclinical development phase.

ORIGINAL DISCOVERIES & MAIN CONTRIBUTIONS TO CANCER RESEARCH

My laboratory at IRB Barcelona is a world reference for the study of colorectal cancer (CRC). We perform basic research using innovative model systems and technologies on topics that are clinically relevant. Our pioneering studies have helped advance the state of the art in several important areas such as the connection between stem cells and cancer, the role of the tumor microenvironment and the identification of mechanisms of metastasis and immune evasion. Some of our discoveries are considered key contributions and have inspired research of many groups worldwide. The impact is reflected in the high number of citations, editorial comments and awards that these studies have received over the past years. Furthermore, some of our latest discoveries have inspired the development of new therapies that are currently being tested in patients through clinical trials. In brief:

1) During my doctoral thesis work I originally identified the transcription factor Snail as a suppressor of E-Cadherin expression in epithelial tumor cells. The Batlle et al. article in **Nature Cell Biology, 2000** (3007 citations) is - together with Cano et al. Nat Cell Biol. 2000 - one of the founding papers of the field on epithelial-to-mesenchymal (EMT) transition in cancer.

2) A major and long-lasting contribution of my research has been linking the biology of intestinal stem cells (ISCs) to CRC development. During my postdoctoral training in the Clevers lab, we originally proposed that the first step towards malignancy in CRC consists in the acquisition of a crypt stem-like phenotype (Batlle et al. Cell. 2002; van de Wetering et al. Cell 2002). This discovery represented the first link between adult ISCs and CRC. Follow-up research carried out in my lab at IRB Barcelona crystallized in several additional important discoveries in this area: **1-** The first purification and “in vitro” expansion of human adult colon stem cells (Jung et al., **Nature Medicine, 2011**). **2-** The characterization of the hierarchical organization of CRC and its relationship to that of the normal colonic mucosa (Merlos-Suárez et al., **Cell Stem Cell, 2011**; Whissell et al., **Nature Cell Biology 2014**; Cortina et al. **EMBO Mol Med. 2017**; Morral et al. **Cell Stem Cell. 2020**). **3 –** The identification of a subpopulation of slow proliferating chemotherapy-resistant ISCs, which are marked by the expression of RNA binding protein Mex3a (Barriga et al. **Cell Stem Cell, 2017**). **4-** The generation of a bi-specific antibody – **MCLA158** - that targets EGFR signaling in LGR5+ cancer stem cells (WO/2017/069628). A paper describing the generation of MCLA-158 has been accepted in principle in **Nature Cancer** pending of minor edits and final editorial checks. This antibody is currently being tested in phase 1 clinical trials for advanced CRC (trial NCT03526835). The first results in patients demonstrated that the antibody is well tolerated. In a cohort of HNSCC patients, interim clinical data showed that the seven patients recruited obtained benefits from MCLA-158 treatment, including two showing partial responses and one achieving a complete

response at data cut-off (see https://merus.nl/wp-content/uploads/2021/10/P185_MCLA-158-HNSCC_virtual-poster_10Sep21_2.pdf). Given that these patients had previously progressed after multiple lines treatment, the responses triggered by MCLA-158 are very significant. Encouraged by these results, the clinical trial continues to recruit patients.

3) My lab pioneered the study of Eph/ephrin signaling in the compartmentalization of normal crypt cells and of CRC cells. The tyrosine kinase receptors Eph and their ligands, the ephrins, were first described as axon pathfinding molecules and their roles had been mainly studied during embryo development. We originally discovered that EphB receptors impose boundaries to the migration of epithelial cells in the intestine and also limit the expansion of colorectal cancers. Subsequently we worked out a downstream mechanism of cell repulsion and differential adhesion triggered by Eph/ephrin interactions in epithelial cells (Batlle et al. ***Cell* 2002**; Batlle et al. ***Nature* 2005**; Cortina et al. ***Nature Genetics* 2007**; Solanas et al. ***Nature Cell Biology* 2011**). These works have inspired many laboratories worldwide to study the role of Eph/ephrin signalling in the physiology of other adult tissues and in the development of multiple cancer types.

4) We discovered that metastasis in CRC is a cancer cell non-autonomous process that depends on a TGF-beta-driven gene program expressed in stromal cells. This phenomenon is the central feature of poor prognosis CRC molecular subtypes (Calon et al. ***Cancer Cell* 2012**; Calon et al. ***Nature Genetics* 2015**). As described in this proposal, we recently developed a pre-clinical model of metastatic CRC that reproduces key features of poor prognosis CRC subtypes developed by patients (Tauriello et al. ***Nature* 2018**). By exploiting this model, we discovered that elevated TGF-beta levels promote T cell exclusion and limit immune responses in metastatic CRC. Recent evidences suggest that this is a general mechanism of immune evasion co-opted by multiple tumor types. Importantly, we showed that therapies that combine TGF-beta inhibitors and immune checkpoint blockade eradicate metastatic disease in our CRC model systems. This combinatorial therapy is inspiring several clinical trials, some of which are already being implemented. In addition, my laboratory has developed a prognostic test – Colostage - that serves as Companion Diagnostics for the therapeutic use of TGF-beta signaling inhibitors (patent WO/2014/072517, PCT/EP2020/077270 and PCT/EP2020/077272). The lab is also involved in generating additional therapeutic tools to target the tumor microenvironment in collaboration with the pharmaceutical industry.

COMPLETE LIST OF PUBLICATIONS (2021-2011 period)

- 1: Tauriello DVF, Sancho E, **Batlle E**. *Overcoming TGF β -mediated immune evasion in cancer*. Nat Rev Cancer. 2022 Jan;22(1):25-44. doi: 10.1038/s41568-021-00413-6. Epub 2021 Oct 20.
- 2: Nieto P, Elosua-Bayes M, Trincado JL, Marchese D, Massoni-Badosa R, Salvany M, Henriques A, Nieto J, Aguilar-Fernández S, Mereu E, Moutinho C, Ruiz S, Lorden P, Chin VT, Kaczorowski D, Chan CL, Gallagher R, Chou A, Planas-Rigol E, Rubio-Perez C, Gut I, Piulats JM, Seoane J, Powell JE, **Batlle E**, Heyn H. *A single-cell tumor immune atlas for precision oncology*. Genome Res. 2021 Oct;31(10):1913-1926. doi: 10.1101/gr.273300.120.
- 3: Vera-Otarola J, Castillo-Vargas E, Angulo J, Barriga FM, **Batlle E**, Lopez-Lastra M. *The viral nucleocapsid protein and the human RNA-binding protein Mex3A promote translation of the Andes orthohantavirus small mRNA*. PLoS Pathog. 2021 Sep 21;17(9):e1009931. doi: 10.1371/journal.ppat.1009931..
- 4: Pérez-González C, Ceada G, Greco F, Matejčić M, Gómez-González M, Castro N, Menendez A, Kale S, Krndija D, Clark AG, Gannavarapu VR, Álvarez-Varela A, Roca- Cusachs P, **Batlle E**, Vignjevic DM, Arroyo M, Trepas X. *Mechanical compartmentalization of the intestinal organoid enables crypt folding and collective cell migration*. Nat Cell Biol. 2021 Jul;23(7):745-757. doi: 10.1038/s41556-021-00699-6.
- 5: Altay G, **Batlle E**, Fernández-Majada V, Martinez E. *In vitro Self-organized Mouse Small Intestinal Epithelial Monolayer Protocol*. Bio Protoc. 2020 Feb 5;10(3):e3514. doi: 10.21769/BioProtoc.3514.
- 6: Kasashima H, Duran A, Cid-Diaz T, Muta Y, Kinoshita H, **Batlle E**, Diaz-Meco MT, Moscat J. *Mouse model of colorectal cancer: orthotopic co-implantation of tumor and stroma cells in cecum and rectum*. STAR Protoc. 2021 Jan 22;2(1):100297. doi: 10.1016/j.xpro.2021.100297.
- 7: Grinat J, Heuberger J, Vidal RO, Goveas N, Kosel F, Berenguer-Llargo A, Kranz A, Wulf-Goldenberg A, Behrens D, Melcher B, Sauer S, Vieth M, **Batlle E**, Stewart AF, Birchmeier W. *The epigenetic regulator Mll1 is required for Wnt-driven intestinal tumorigenesis and cancer stemness*. Nat Commun. 2020 Dec 21;11(1):6422. doi: 10.1038/s41467-020-20222-z.
- 8: Kasashima H, Duran A, Martinez-Ordoñez A, Nakanishi Y, Kinoshita H, Linares JF, Reina-Campos M, Kudo Y, L'Hermitte A, Yashiro M, Ohira M, Bao F, Tauriello DVF, **Batlle E**, Diaz-Meco MT, Moscat J. *Stromal SOX2 Upregulation Promotes Tumorigenesis through the Generation of a SFRP1/2-Expressing Cancer-Associated Fibroblast Population*. Dev Cell. 2021 Jan 11;56(1):95-110.e10. doi: 10.1016/j.devcel.2020.10.014.
- 9: Morral C, Stanisavljevic J, **Batlle E**. *Protocol for Efficient Protein Synthesis Detection by Click Chemistry in Colorectal Cancer Patient-Derived Organoids Grown In Vitro*. STAR Protoc. 2020 Sep 18;1(2):100103. doi: 10.1016/j.xpro.2020.100103.
- 10: Urošević J, Blasco MT, Llorente A, Bellmunt A, Berenguer-Llargo A, Guiu M, Cañellas A, Fernandez E, Burkov I, Clapés M, Cartanà M, Figueras-Puig C, **Batlle E**, Nebreda AR, Gomis RR. *ERK1/2 Signaling Induces Upregulation of ANGPT2 and CXCR4 to Mediate Liver Metastasis in Colon Cancer*. Cancer Res. 2020 Nov 1;80(21):4668-4680. doi: 10.1158/0008-5472.CAN-19-4028.
- 11: Mereu E, Lafzi A, Moutinho C, Ziegenhain C, McCarthy DJ, Álvarez-Varela A, **Batlle E**, Sagar, Grün D, Lau JK, Boutet SC, Sanada C, Ooi A, Jones RC, Kaihara K, Brampton C, Talaga Y, Sasagawa Y, Tanaka K, Hayashi T, Braeuning C, Fischer C, Sauer S, Trefzer T, Conrad C, Adiconis X, Nguyen LT, Regev A, Levin JZ, Parekh S, Janjic A, Wange LE, Bagnoli JW, Enard W, Gut M, Sandberg R, Nikaido I, Gut I, Stegle O, Heyn H. *Benchmarking single-cell RNA-sequencing protocols for cell atlas projects*. Nat Biotechnol. 2020 Jun;38(6):747-755. doi: 10.1038/s41587-020-0469-4.

- 12: Morral C, Stanisavljevic J, Hernando-Momblona X, Mereu E, Álvarez-Varela A, Cortina C, Stork D, Slebe F, Turon G, Whissell G, Sevillano M, Merlos-Suárez A, Casanova-Martí À, Moutinho C, Lowe SW, Dow LE, Villanueva A, Sancho E, Heyn H, **Batlle E**. *Zonation of Ribosomal DNA Transcription Defines a Stem Cell Hierarchy in Colorectal Cancer*. Cell Stem Cell. 2020 Jun 4;26(6):845-861.e12. doi:10.1016/j.stem.2020.04.012.
- 13: Altay G, Larrañaga E, Tosi S, Barriga FM, **Batlle E**, Fernández-Majada V, Martínez E. *Author Correction: Self-organized intestinal epithelial monolayers in crypt and villus-like domains show effective barrier function*. Sci Rep. 2019 Dec 6;9(1):18822. doi: 10.1038/s41598-019-55181-z. Erratum for: Sci Rep. 2019 Jul 12;9(1):10140.
- 14: Fernández-Barral A, Costales-Carrera A, Buira SP, Jung P, Ferrer-Mayorga G, Larriba MJ, Bustamante-Madrid P, Domínguez O, Real FX, Guerra-Pastrián L, Lafarga M, García-Olmo D, Cantero R, Del Peso L, **Batlle E**, Rojo F, Muñoz A, Barbáchano A. *Vitamin D differentially regulates colon stem cells in patient-derived normal and tumor organoids*. FEBS J. 2020 Jan;287(1):53-72. doi: 10.1111/febs.14998. Epub 2019 Jul 29.
- 15: Altay G, Larrañaga E, Tosi S, Barriga FM, **Batlle E**, Fernández-Majada V, Martínez E. *Self-organized intestinal epithelial monolayers in crypt and villus-like domains show effective barrier function*. Sci Rep. 2019 Jul 12;9(1):10140. doi: 10.1038/s41598-019-46497-x. Erratum in: Sci Rep. 2019 Dec 6;9(1):18822.
- 16: Campbell K, Rossi F, Adams J, Pitsidianaki I, Barriga FM, Garcia-Gerique L, **Batlle E**, Casanova J, Casali A. *Collective cell migration and metastases induced by an epithelial-to-mesenchymal transition in Drosophila intestinal tumors*. Nat Commun. 2019 May 24;10(1):2311. doi: 10.1038/s41467-019-10269-y.
- 17: **Batlle E**, Massagué J. *Transforming Growth Factor- β Signaling in Immunity and Cancer*. Immunity. 2019 Apr 16;50(4):924-940. doi: 10.1016/j.immuni.2019.03.024.
- 18: Tauriello DVF, Palomo-Ponce S, Stork D, Berenguer-Llargo A, Badia-Ramentol J, Iglesias M, Sevillano M, Ibiza S, Cañellas A, Hernando-Momblona X, Byrom D, Matarin JA, Calon A, Rivas EI, Nebreda AR, Riera A, Attolini CS, **Batlle E**. *TGF β drives immune evasion in genetically reconstituted colon cancer metastasis*. Nature. 2018 Feb 22;554(7693):538-543. doi: 10.1038/nature25492. Epub 2018 Feb 14.
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OUTREACH ACTIVITIES AND MEDIA COVERAGE (selection of recent)

- Different media, including main TV channels and newspapers, have covered the activity and discoveries of the lab over the past years. Two selected examples amongst of dozens of newspapers articles are;

<https://www.lavanguardia.com/ciencia/20180214/44782658824/inmunoterapia-esperanza-cancer-colon-tgf-beta.html>

<https://elpais.com/ciencia/2021-11-26/nadie-entiende-por-que-los-jovenes-tienen-cada-vez-mas-cancer-de-colon.html>

- Crazy in Biomedicine. Catalunya La Pedrera Foundation. My lab has participated in 3 editions tutoring school students in their last year on Saturdays into some of the research projects carried out in the laboratory.

<https://bojos-ciencia.fundaciocatalunya-lapedrera.com/cursos/biomedicine>

- Women scientists (2021): <https://www.donesciencia.cat/100tifiques/>

- 2019 Edition of the pint of Science” Festival: Hacking cancer: Jordi Badía: Immunotherapy: how to fight cancer with our defenses. <https://pintofscience.es/event/hackeando-el-cancer>

- 2018 Edition of the pint of Science” Festival: Genetic Edition: What is Crispr? Gemma Turon: Modifying genes to understand colon cancer. <https://pintofscience.es/event/edicin-gentica-qu-es-crispr>

<https://www.elperiodico.com/es/ciencia/20180515/pint-of-science-18-ciencia-bares-cerveza-6820801>

- Design of a “Scientific” Escape Room at IRB Barcelona:

<https://www.lavanguardia.com/vida/20190628/463144362124/organizan-un-escape-room-para-financiar-la-investigacion-de-la-metastasis.html>

- Generation of a youtube video explaining the results obtained in the Tauriello et al. paper in Nature 2018 (EN & and ESP> more than 12000 views):

<https://www.youtube.com/watch?v=Yg1NTdoC8JU>

<https://www.youtube.com/watch?v=FdSvydBWV0>

- Outreach Youtube Science Snacks - "ELS ORGANOIDES" - Maria Salvany

<https://www.youtube.com/watch?v=cB7PtEyl3Ho&t=4s>

- Participation in the event organized by the ESADE business school together with IRB Barcelona "Metastasis challenge: from research to social impact" by Eduard Batlle:

<https://www.irbbarcelona.org/es/news/joan-massage-apela-a-hacer-de-la-investigacion-en-metastasis-un-reto-de-toda-la-sociedad>

- Dissemination Conference and participation in various events on IRB Barcelona Open Doors. Eduard Batlle. <https://www.irbbarcelona.org/en/public-engagement/general-public/jornada-de-portes-obertes-2019> <https://www.youtube.com/watch?v=UuR-15q4afk>

- Dissemination Conference at the VilaPensa 2018 festival: Elena Sancho: Oncology: The immunooncology, the new strategy in the rain against cancer.

http://vilapensa.cat/wp-content/uploads/2018/04/ViPe_programa_Web.pdf

- Banc Sabadell Forum Dissemination Conference: Elena Sancho: The new strategy in the fight against cancer.

<https://www.youtube.com/watch?v=2tgrQusBmq4>

In addition, we promote our research through institutional website and Twitter:

@IRB Barcelona 16,100 followers;

@BatlleLab 1400 followers

Barcelona, January 11th, 2022

A handwritten signature in blue ink, consisting of stylized, overlapping loops and a horizontal line, likely representing the name 'Eduard Batlle'.

Signed, Eduard Batlle