



Call for PhD research projects 2015-2018

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Ongoing PhD student supervision: 0
Name and date of first registration of each PhD student:

Name and viva date of each PhD student you supervised during the last 5 years:

Title of the PhD project : Optimization and mechanism of action of therapeutic mAb anti-CLDN1

Thesis project:

We have recently shown that claudin 1 (Cldn1), a transmembrane protein, main component of tight junctions, is overexpressed in colorectal cancer (CRC) and that Cldn1 overexpression is associated with a shorter survival. After production of mAb anti-CLDN1, we demonstrated that Cldn1 is a new therapeutic target for antibody based therapy in CRC. Indeed, mAb-targeting Cldn1 caused a significant decrease of growth, migration and invasion of tumor cells as well *in vivo* as *in vitro*.

We made a proof of concept that targeting Cldn1 by a mAb had a therapeutic effect in colorectal cancer. The aim of the proposed thesis topic, is now, to better characterize the interaction Cldn1 / Acm anti-CLDN1, to increase the efficiency of this mAb, to evaluate its toxicity and to understand its mechanism of action.

5 publications

Thierry AR, Mouliere F, El Messaoudi S, Mollevi C, Lopez-Crapez E, Rolet F, Gillet B, Gongora C, Dechelotte P, Robert B, **Del Rio M**, Lamy PJ, Bibeau F, Nouaille M, Lorient V, Jarrousse AS, Molina F, MATHONNET M, Pezet D, Ychou M. Clinical validation of the detection of KRAS and BRAF mutations from circulating tumor DNA. *Nat Med.* 2014 Apr;20(4):430-5.

Sadanandam A, Lyssiotis CA, Homicsko K, Collisson EA, Gibb WJ, Wullschleger S, Ostos LC, Lannon WA, Grotzinger C, **Del Rio M**, Lhermitte B, Olshen AB, Wiedenmann B, Cantley LC, Gray JW, Hanahan D. A colorectal cancer classification system that associates cellular phenotype and responses to therapy. *Nat Med.* 2013 May;19(5):619-25.

Del Rio M, Mollevi C, Vezzio-Vie N, Bibeau F, Ychou M, Martineau P. Specific extracellular matrix remodeling signature of colon hepatic metastases. *PLoS One.* 2013 Sep 4;8(9):e74599.

Gongora C, Vezzio-Vie N, Tuduri S, Denis V, Causse A, Auzanneau C, Collod-Beroud G, Coquelle A, Pasero P, Pourquier P, Martineau P, **Del Rio M**. New Topoisomerase I mutations are associated with resistance to camptothecin. *Mol Cancer.* 2011 May 27;10:64.

Paillas S, Boissière F, Bibeau F, Denouel A, Mollevi C, Causse A, Denis V, Vezzio-Vié N, Marzi L, Cortijo C, Ait-Arsa I, Askari N, Pourquier P, Martineau P, **Del Rio M**, Gongora C. Targeting the p38 MAPK pathway inhibits irinotecan resistance in colon adenocarcinoma. *Cancer Res.* 2011 Feb 1;71(3):1041-9.