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RNA BIOLOGY, SIGNALING AND CANCER

Our team focuses on the role of RNA regulations and RNA-binding proteins in cancer biology and anticancer therapy.

We study several aspects of RNA regulations and RNA-binding proteins: - post-transcriptional gene regulation (i.e. intronic polyadenylation, translation), - both canonical and non-canonical RNA-binding proteins, - long non-coding RNAs.

We study several aspects of cancer biology and anticancer therapies: - genome instability and genotoxic chemotherapy, - oncogenic signaling pathways and targeted therapies, - cancer-immune cells cross-talk and immunotherapy.

We study several cancers: - cutaneous melanoma, - breast cancer, - acute T lymphoblastic leukemia, - non-small cell lung cancer.

To tackle these issues, we use a combination of approaches: - biochemical analyses of RNA, proteins and their interactions, - genome-wide analyses of RNA regulations (RNA-seq, 3' seq, polysome profiling) and RNA-protein interactions (iCLIP), - analyses of cancer cell phenotypes in cell culture, - tumor biology *in vivo* and patients tumors.

Ongoing projects:

Axis 1: Control of genome stability and genotoxic response. 1.1- Regulation of intronic polyadenylation in response/ resistance to genotoxic agents. 1.2- Interaction between DNA-damage response proteins and RNA.

Axis 2: Tumor-intrinsic mechanisms of resistance to targeted therapies. 2.1- Dynamic reprogramming of mRNA translation in drug-tolerant cancer cells. 2.2- Direct Interaction between MAPK signaling proteins and RNAs.

Axis 3: Crosstalk between tumor cells and their environment. 3.1- T cell receptor-dependent gene regulation in acute T lymphoblastic leukemia. 3.2- Immune-dependent post-transcriptional gene regulation in melanoma. 3.3- Immunotherapies.

Six key publications (since 2014)

(*co-corresponding authors, #co-first authors)

Shen S, Faouzi S, Bastide A, Martineau S, Malka-Mahieu H, Fu Y, Sun X, Mateus C, Routier E, Roy S, Desaubry L, André F, Eggermont A, David A, Scoazec JY, Vagner S*, Robert C* (2020). [An epitranscriptomic mechanism underlies selective mRNA translation remodelling in melanoma persister cells.](#) **Nat Commun.** 16;10(1):5713.

Tanaka I, Chakraborty A, Saulnier O, Benoit-Pilven C, Vacher S, Labiod D, Lam EWF, Bièche I, Delattre O, Pouzoulet F, Auboeuf D, Vagner S, Dutertre M. (2020). [ZRANB2 and SYF2-mediated splicing programs converging on ECT2 are involved in breast cancer cell resistance to doxorubicin.](#) **Nucleic Acids Res.** 18;48(5):2676-2693.

Cerezo M#, Guemiri R#, Druillennec S, Girault I, Malka-Mahieu H, Shen S, Allard D, Martineau S, Welsch C, Agoussi S, Estrada C, Adam J, Libenciuc C, Routier E, Roy S, Desaubry L, Eggermont AM, Sonenberg N, Scoazec JY, Eychène A, Vagner S*, Robert C*. (2018) [Translational control of tumor immune escape via the eIF4F-STAT1-PDL1 axis in melanoma.](#) **Nat Med**, 24:1877-1886

Trinquand A#, Dos Santos NR#, Tran Quang C#, Rocchetti F, Zaniboni B, Belhocine M, Da Costa De Jesus C, Lhermitte L, Tesio M, Dussiot M, Cosset F, Verhoeyen E, Pflumio F, Ifrah N, Dombret H, Spicuglia S, Chatenoud L, Gross DA, Hermine O, Macintyre E, Ghysdael J*, Asnafi V* (2016) [Triggering The Tcr Developmental Checkpoint Activates A Therapeutically Targetable Tumor Suppressive Pathway In T-Cell Leukemia.](#) **Cancer Discov**, 6:972-985.

Passaro D, Irigoyen M, Catherinet C, Gachet S, Da Costa De Jesus C, Lasgi C, Tran Quang C, Ghysdael J (2015). [CXCR4 Is Required For Leukemia Initiating Cell Activity In T-Cell Acute Lymphoblastic Leukemia.](#) **Cancer Cell**, 27:769-779.

Boussemart, L., Malka-Mahieu, H., Girault, I., Allard, D., Hemmingsson, O., Tomasic, G., Thomas, M., Basmadjian, C., Ribeiro, N., Thuaud, F., Mateus, C., Routier, E., Kamsu-Kom, N., Agoussi, S., Eggermont, A. M., Desaubry, L., Robert, C.*, and Vagner, S.* (2014) [eIF4F is a nexus of resistance to anti-BRAF and anti-MEK cancer therapies.](#) **Nature**, 513:105-109

Key publications

Year of publication 2017

Michelle Newman, Rym Sfaxi, Abhijit Saha, David Monchaud, Marie-Paule Teulade-Fichou, Stéphan Vagner (2017 Oct 27)

The G-Quadruplex-Specific RNA Helicase DHX36 Regulates p53 Pre-mRNA 3'-End Processing Following UV-Induced DNA Damage.

Journal of Molecular Biology : 429 : 3121-3131 : [DOI : 10.1016/j.jmb.2016.11.033](https://doi.org/10.1016/j.jmb.2016.11.033)

Year of publication 2016

Anne Cammas, Magali Lacroix-Triki, Sandra Pierredon, Morgane Le Bras, Jason S Iacovoni, Marie-Paule Teulade-Fichou, Gilles Favre, Henri Roché, Thomas Filleron, Stefania Millevoi, Stéphan Vagner (2016 Mar 29)

hnRNP A1-mediated translational regulation of the G quadruplex-containing RON receptor tyrosine kinase mRNA linked to tumor progression.

Oncotarget : 7 : 16793-16805 : [DOI : 10.18632/oncotarget.7589](https://doi.org/10.18632/oncotarget.7589)