

## Contact Details

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## Research interests:

Stéphanie Plenchette is a principal investigator at LIIC who focuses on exploiting nitric oxide (NO), particularly the NO-releasing drug glyceryl trinitrate (GTN), to enhance the efficacy of cancer therapeutics (e.g. for colorectal cancer and triple-negative breast cancer). Specifically, she conducts research related to inflammation, cytokines and cancer. The inflammatory response is a tightly regulated event that implies a highly interrelated network of distinct cells within the tumor microenvironment (immune and non-immune cells) and signalling pathways (cytokines pathways). Stéphanie Plenchette's research interests particularly focuses on studying the regulatory role of NO in a chemo-induced inflammatory microenvironment.

Signalling pathways mediated by the Tumor Necrosis Factor (TNF) ligands and other important proinflammatory cytokines of the tumor microenvironment such as IL-6 are at the core of the research projects. TNF ligands (TNF $\alpha$ , FasL and TRAIL) are major inflammatory and immunoregulatory cytokines that play paradoxical functions, either sustaining prosurvival/proinflammatory signalling or prodeath signalling pathways.

Much of the effort is directed towards better understanding protein S-nitrosylation which largely influences cellular signaling outcomes in cancer, specifically cancer cell death or metastasis formation. S-nitrosylation is a reversible protein post-translation modification induced by NO and a dynamic process that can exert opposite effects on cancer disease. New strategies based on NO, harnessing the cytokines of the tumor microenvironment, aim at developing new therapeutic options. Therefore, the purpose of this research programme is to better delineate the anti-tumor mode of action of GTN and the appropriate use of GTN in combined therapy.

## Slected publication

1. Mabrouk N, Ghione S, Laurens V, **Plenchette S**, Bettaieb A, Paul C. Senescence and cancer: role of nitric oxide (NO) in SASP. (2020) *Cancers (Basel)*. 2;12(5):1145.
2. Ghione S, Mabrouk N, Paul C, Bettaieb A, **Plenchette S**. Protein kinase inhibitor-based cancer therapies: considering the potential of nitric oxide (NO) to improve cancer treatment. (2020) *Biochem Pharmacol*. 176:113855.
3. Bouaouiche S, Magadoux L, Dondaine L, Reveneau S, Isambert N, Bettaieb A, Jeannin JF, Laurens V, **Plenchette S**. Glyceryl trinitrate-induced cytotoxicity of docetaxel-resistant cancer cells is associated with differential regulation of clusterin. (2019) *Int J Oncol*. 54(4):1446-1456.
4. Romagny S, Bouaouiche S, Lucchi G, Ducoroy P, Bertoldo J, Terenzi H, Bettaieb A, **Plenchette S**. S-nitrosylation of cIAP1 switches cancer cell fate from TNF $\alpha$ /TNFR1-mediated cell survival to cell death. (2018) *Cancer Res*. 78(8):1948-1957.
5. Bettaieb A, Paul C, **Plenchette S**. Exploration of Fas S-nitrosylation by the Biotin Switch Assay. (2017) *Methods Mol Biol*. 1557:199-206.
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7. Bouaouiche S, Dubrez L, Bettaieb A, **Plenchette S**. IAPs : mediators of oncogenesis and targets for anticancer therapy. (2016) *Crit Rev Oncog*. 21(5-6):399-411.
8. **Plenchette S**, Romagny S, Laurens V, Bettaieb A. NO and cancer: itinerary of a double agent. NO et cancer: itinéraire d'un agent double. (2016) *Med Sci*. 32(6-7):625-33.
9. **Plenchette S**, Romagny S, Laurens V, Bettaieb A. S-nitrosylation in TNF superfamily signaling pathway: implication in cancer. (2015) *Redox. Biol*. 6:507-15.
10. Magadoux L, Isambert N, **Plenchette S**, Jeannin JF and Laurens V. (2014). Emerging targets to monitor and overcome docetaxel resistance in castration resistant prostate cancer. *Int J Oncology*. 45(3):919-28.
11. Marivin A, Berthelet J, **Plenchette S**, and Dubrez, L. The Inhibitor of Apoptosis (IAPs) in Adaptive Response to Cellular Stress. (2012) *Cells*. 1, 711-737.
12. Cartier J, Berthelet J, Marivin A, Gemble S, Edmond V, **Plenchette S**, Lagrange B, Hammann A, Dupoux A, Delva L, Eymin B, Solary E, Dubrez L. cellular inhibitor of apoptosis protein-1 (cIAP1) can regulate e2F1-mediated control of cyclin transcription. (2011) *J Biol Chem*. 29;286(30):26406-17.

13. Leon-Bollotte L, Subramaniam S, Cauvard O, **Plenquette-Colas S**, Paul C, Godard C, Martinez-Ruiz A, Legembre P, Jeannin JF, and Bettaieb A. S-nitrosylation of the death receptor Fas amplifies Fas ligand-mediated cancer cell apoptosis. (2011) *Gastroenterology* 140(7):2009-18.