DRUG REPURPOSING: SULFASALAZINE AS A NEW ANTICANCER TREATMENT. STUDY OF TUMOUR DRUG DISTRIBUTION THROUGH PET AND MRI IMAGING

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Glioblastoma is among the deadliest cancers and treatment with radiotherapy has a high chance of failure due to the presence of Glutathione (GSH), one of the most important cellular defensive tools. Recent studies proved that Sulfasalazine (SAS), an old drug used for ulcerative colitis and Crohn's disease, could be repurposed for the treatment of radiotherapy-resistant glioblastomas for its ability to stop GSH biosynthesis. [1]

SAS activity has been confirmed both *in vitro* and in preliminary *in vivo* studies. To further validate this approach, new pharmacological analyses have to be conducted; especially in regards with the blood-brain barrier permeability and the metabolic stability. Aiming for a better understanding of SAS biological behavior, imaging techniques, such as PET and MRI, are needed to investigate the pharmacokinetic properties in the least invasive and most direct way.

In this project, we are working on the SAS radiolabeling as ^{11}C and ^{13}C isotopes employing diazocopulation and Miyaura borylation or Sandmeyer-like borylation for the cold chemistry and an oxidative hydroxycarbonylation for the radiolabeling step. [2] (Figure 1)

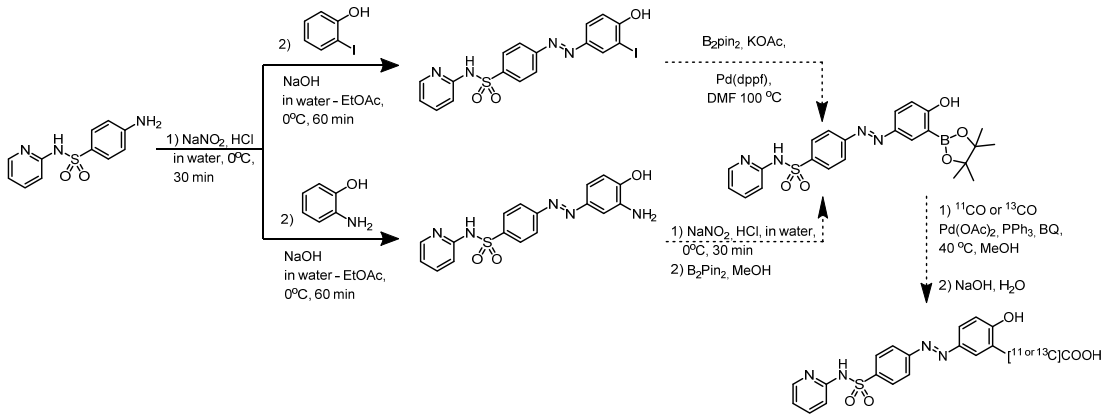

Figure 1. Sulfasalazine ^{11}C and ^{13}C syntheses

After the isolation of the ^{11}C and ^{13}C probes, these molecules will be tested for *in vivo* studies to assess SAS biological behavior and the feasibility of this new approach that combines chemotherapy with radiotherapy.

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[1] Sleire, L., Skeike, B.S.; Enger, P.Ø. and al., *Oncogene*, **2015**, 34, 5951-5959

[2] a. Ishii, A.; Mineghishi, K.; Nagatsu, K.; Zhang, M.R.; *Tetrahedron*, **2015**, 71, 1588-1596. b. Yamamoto, Y.; *Adv. Synth. Catal.*, **2010**, 352, 478-492.