



MEDICAL ONCOLOGY AND HEMATOLOGY

Project title

“Analysis of combined assessment of metabolic radiomics pattern in [18]F-FDG-PET/CT, Immunogenic Cell Death induction and microbiota in the prediction of response to neoadjuvant chemotherapy in breast cancer patients: a proof-of-concept study”

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Abstract

The program will investigate predictive factors of response to neoadjuvant chemotherapy (NAC) in locally advanced breast cancer (BC). Individual response depends on a complex tumor-host interaction. Microbiota is the ensemble of commensal bacteria and has been proven to be related to cancerogenesis, through its direct and indirect action on immunogenic cell death (ICD). Microbiota has been identified in extra gut sites, as breast milk and tissue, possibly influencing the immune-metabolic profile of BC cells.

Among research and clinical activities, breast, oral and intestinal microbiota will be analyzed; ICD markers will be detected on plasma samples and in tumor tissue; a metabolic study with [18]F-FDG PET/CT through radiomics analysis will be performed.

We plan to see if PET radiomic patterns can predict response, if microbiota features obtained by biopsies of a cohort of BC patients correlate with radiomic textures through a mechanism linking the two by means of ICD.

Main technical approaches

Tumor burden will be delineated on [18]F-FDG PET/CT images on baseline and after NAC (if residual metabolic activity will persist) by a semi-quantitative approach, and quantitative parameters will be extracted.

ICD markers: blood samples will be taken before and within day 4 after first administration of NAC. Quantification of HMGB1 in plasma samples will be assessed by an ELISA kit.

RNAseq analysis: tumor biopsies, collected before NAC, and tumor specimens (or tumor bed of pathological Complete Response patients) after NAC will be frozen directly in Trizol. Total RNA will be extracted from the biopsies collected before the treatment. mRNA-Seq library preparation will be performed with the TruSeq RNA Sample Prep kit and sequenced.

Microbiota analysis: BC biopsies (collected before NAC), oral and fecal samples (collected before and at the end of NAC) will be frozen. Bacterial DNA will be extracted and amplified for 16S rRNA sequencing.

Scientific references

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Lee SS et al. Correlation of Molecular Subtypes of Invasive Ductal Carcinoma of Breast with Glucose Metabolism in FDG PET/CT: Based on the Recommendations of the St. Gallen Consensus Meeting 2013. Nucl Med Mol Imaging 2017; 51:79-85.

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