



TEMPLATE RICHIESTA ATTIVAZIONE TOPIC AGGIUNTIVI SU FONDI PNRR

D.M. 9 aprile 2022 n. 352

Project title/Titolo del Progetto	Development and validation of imaging tools for the biological characterization of prostate cancer.
Principal Investigator	Arturo Chiti
Main field of interest/Ambito principale di ricerca	Diagnostica e terapie innovative nella medicina di precisione / Innovative diagnostic tools and therapies in precision medicine
Abstract	<p>Radiopharmaceuticals' ability to target essential components of prostate cancer cells is being exploited as a personalized-medicine approach both as a diagnostic tool and as therapeutic strategy for patients with mCRPC or recurrent PCa.</p> <p>The value of small organic ligands for imaging of solid malignancies has been demonstrated in prostate cancer, using prostate-specific membrane antigen (PSMA). Nonetheless, new generation molecules can be improved in terms of diagnostic efficacy and biodistribution. There is room for improvement for modulating the radiopharmaceutical's uptake or accumulation in non-target organs, like the liver, the kidneys, the bladder and the salivary glands.</p> <p>The project aims at evaluating the diagnostic efficacy and safety of new radiolabeled PSMA derivatives. Data on the uptake, biodistribution, pharmacokinetics and excretion of new PSMA derivatives will be collected from existing pre-clinical models and translated in human studies.</p> <p>Moreover, a high affinity moiety could be used to deliver not only diagnostic radionuclides such as ⁶⁸Ga, but also therapeutic radionuclides such as ¹⁷⁷Lu to the tumor, in the concept of theragnostic applications. The clinical part of the PhD project will run under a clinical trial, that will be submitted for approval to the local ethics committee and, if needed, to AIFA. Patients affected by high-risk prostate cancer or by biochemical relapse of prostate cancer after prostatectomy or radical radiotherapy will be the target population to be enrolled. Uptake of the radiopharmaceutical will be assessed and quantified with advanced image analyses techniques, to build a correlation with clinical and pathological data and predict the feasibility of the therapeutical application of the companion radiopharmaceutical.</p>
Type of Co-funding	<ul style="list-style-type: none"> ○ D.M. 352/2022 - Borse di dottorato cofinanziate dalle imprese¹
Lab name and address	Advanced Image Analyses, Humanitas University and Nuclear Medicine Unit, IRCCS Humanitas
Brief description of the coherence of the Project in relation to the PNRR objectives ³	<p>The project will focus on the application in oncology of the theragnostic concept: using a molecule to detect a tumor's target and a compound molecule to hit the target with a local, super selective, radiation therapy. The theragnostic concept fits with the broader concept of precision medicine.</p> <p>The PhD program will run in collaboration with a pharmaceutical</p>



	<p>company, Bracco, that has an established and prominent role in the diagnostic imaging field. The clinical applications will be developed in the Nuclear Medicine Unit of the Humanitas Cancer Center, that has the capabilities of producing radiopharmaceuticals and run clinical trials. The PhD candidate will be motivated to generated data that will be available according to the principles of Open Science.</p> <p>Humanitas University has an international reputation and several connections with well-known Universities. Bracco is an international company with relevant research interests worldwide. This will be an excellent environment for a PhD candidate aiming at building her/his education at a European level.</p> <p>Results of the PhD project will contribute to sustain Italian and European research in the field of radiopharmaceuticals.</p>
N. of months abroad (min. 6, max. 18) [compulsory]	18
Name of the research institution/company abroad	Bracco
N. of months of internship (min. 6, max. 18) [compulsory only for D.M. 352/2022]	18
Name of the company ³	Bracco
Scientific references	<ul style="list-style-type: none"> • Afshar-Oromieh A, Malcher A, Eder M, et al. Pet imaging with a [68ga]gallium-labelled psma ligand for the diagnosis of prostate cancer: Biodistribution in humans and first evaluation of tumour lesions. <i>Eur J Nucl Med Mol Imaging</i>. 2013;40:486–495. • Afshar-Oromieh A, Zechmann CM, Malcher A, et al. Comparison of PET imaging with a 68Ga-labelled PSMA ligand and 18F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. <i>Eur J Nucl Med Mol Imaging</i>. 2014;41:11–20. • Maurer T, Gschwend JE, Rauscher I, et al. Diagnostic efficacy of 68Gallium-PSMA positron emission tomography compared to conventional imaging for lymph node staging of 130 consecutive patients with intermediate to high risk prostate cancer. <i>J Urol</i> [Internet]. Elsevier Ltd; 2016;195:1436–1443. Available from: http://dx.doi.org/10.1016/j.juro.2015.12.025 • Kuten J, Fahoum I, Savin Z, et al. Head-to-head comparison of 68Ga-PSMA-11 with 18F-PSMA-1007 PET/CT in staging prostate cancer using histopathology and immunohistochemical analysis as a reference standard. <i>J Nucl Med</i>. 2020;61:527–532. • Afshar-Oromieh A, Avtzi E, Giesel FL, et al. The diagnostic value of PET/CT imaging with the 68Ga-labelled PSMA ligand HBED-CC in the diagnosis of recurrent prostate cancer. <i>Eur J Nucl Med Mol Imaging</i> [Internet]. 2015;42:197–209. Available from: http://link.springer.com/10.1007/s00259-014-2949-6 • Afshar-Oromieh A, Holland-Letz T, Giesel FL, et al. Diagnostic performance of 68Ga-PSMA-11 (HBED-CC) PET/CT in patients with recurrent prostate cancer: evaluation in 1007 patients. <i>Eur J Nucl Med Mol Imaging</i>. <i>European Journal of Nuclear Medicine and Molecular Imaging</i>; 2017;44:1258–1268. • Fendler WP, Calais J, Eiber M, et al. Assessment of 68Ga-PSMA-



	<p>11 PET Accuracy in Localizing Recurrent Prostate Cancer: A Prospective Single-Arm Clinical Trial. JAMA Oncol. 2019;5:856–863.</p> <p>Afshar-romieh A, Livorsi M, Wagner J, et al. Performance of [68 Ga] Ga-PSMA-11 PET / CT in patients with recurrent prostate cancer after prostatectomy — a multi-centre evaluation of 2533 patients. European Journal of Nuclear Medicine and Molecular Imaging; 2021;2925–2934.</p>
Type of contract	<p>PhD scholarship of € 18.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.</p>