

Project 8

the PhD course Prof. Maria Triassi Coordinator Microbiome as predictive factor in cancer immunotherapy the PhD project Department of Public Health reference The Department of Public Health cordinator The Department of Public Health cordinator The Department of Public Health carries out transitional activity. Patient care is carried out in a wide range of Clinical Institutes, such as Surgery orthopedica, Anatomic Pathology, Endocrinology, Rephrology, Reprocedogy, and Cocupational Medicine. Novel therapeutic approaches are developed on mouse and human models. Investigation is carried out in several departmental to biotorioris, that are fully equipped with luminometers, Sike Bad imaging system, Nanodrog and Aglient spectrometers, various Nikon and Zeiss immunofluorescence and confocal microscopes and PLC. Available instruments include cryotast. Lisuse embedding station, ten microtones, as well as several dissecting microscopes for molecular microbiology and molecular cryopathology as well as fully automated net generations instruments include cryotast. Ling, protoxoa, archive and biotary pregramentation in clinical practice of novel diagnostic, prognostic and predictive disease biomarkers Scientific 3 Scientific 3 Scientific 3 The human body represents a really complex ecosystem comprised of 30 trillion cells inhabited by approximately a provide the bast. In addition, the microbiota and bus well as fully automated in modularing the efficacy and toxicity, a carured by the bast. In addition, the microbiota and be wery useful, in combination with other well standardized biomarkers, such as PD – 11 expression evaluation, to improve the efficacy of cancer patient salecular in the contents and incrobiota. The microbiota is scapable of synthesizing or transforming a large number of mediatorise. Toris, and and PD i Immune-checkpoint to microbiota and sequences and volus extended in the commensal microbiota. The microbiota is scapable of synthesizing or transforming a large number of mediatolites, which cannon badd and den	Name/title of	Public Health and Preventive Medicine
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Project Research plan Four different research and training main phases: A1. Panel Design; A2. In silico validation, A3. In vitro validation A4. Patients sample collection and clinical evaluation. A series of 24 NSCLC cancer patients treated with Pembrolizumab in monotherapy in first line of treatment, with histologically confirmed adenocarcinoma will be characterized for microbiome status. Fecal samples will be collected from each patients and DNA will be extracted by using PureLinkTM Microbiome DNA Purification Kit (PL; Thermo Fisher Scientific) following the manufacturer procedure and analyzed by using the developed and in vitro validated multiplex barcode color code panel. The obtained results will be matched with the clinical data to assess the predictive value of our customized panel. In particular Objective Response Rate and Progression Free Survival at 12 months will be validated in future prospective studior.		blockade therapies.
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I SLUURS.		studies.



Research and Training Innovative aspects	Currently, the selective amplification and sequencing of part of the gene encoding the 16S rRNA represent the most common method for taxonomic characterization of complex bacterial communities. On the overall, a pair of universal primers targeting conserved sequences flanking a hypervariable region are used to generate an amplicon library, which is then sequenced. Because bacterial identification is based on a portion of the 16S rRNA gene sequencing species level resolution is usually not feasible with this method. In addition, most bacteria contain
	multiple copies of the 16S rRNA gene, which can lead to inaccurate quantitation of bacterial cells. Also the amplification step represent an additional bias and is strictly depended on the primers choice. Metagenomic shotgun sequencing is considered less biased than 16S rRNA gene amplicon sequencing, because it does not contain a PCR amplification step. However, this can result in contamination with human genomic DNA and requires higher sequence coverage to detect bacterial species of low abundance. This necessitates additional data storage,
	analysis at the step of genome assembly or gene prediction. Another important limitation of metagenomic shotgun sequencing is related to the functional capacity definition, in fact functional capacity can only be inferred indirectly from 16S rRNA amplicon sequencing data.Our project proposal will allow the overcome of these limits by using an innovative specific "microbiome panel" for precise characterization of the microbiota based on a multiplex digital colour-coded barcode hybridization technology (NanoString Technologies, Seattle, Washington, USA) approach
	which gives the possibility to simultaneously analyze in a single-tube multiplexed fashion a broad spectrum of DNA fragments on different biological specimens, across all levels of biological expression. This approach provides a method for direct detection of targets with fluorescent molecular barcoded probes without the need of reverse transcription and/or amplification.
Inter-	This project will involve four different area of expertise, in particular:
Multidisciplinary	Predictive Molecular Pathology: Design, develop and validation of next generation technology based approach to
aspects	analyze quality and quantity of microbiome. In particular a multiplex color code barcode technology will be evaluated to assess the microbiome in cancer patients derived samples. Bioinformatics: a dedicated pipeline, based
	on nSolver 3.0 software will be customized to analyze the data obtained by using the custom multiplex color code
	barcode probe set. Anatomic Pathology: Cytological or histological confirmed lung adenocarcinoma patients will be
	recruited for this study. Oncology: Patient treated in monotherapy with Pembrolizumab in first line of treatment
	with complete clinical records to assess Objective Response Rate and Progression Free Survival evaluated by an
Consudations	experienced oncologist will be recruited for this study
opportunities	ne onversity of Padda, Department of Medicine Dimed . the fole of MSD will be focused of training for the
opportunities	PANGAFA BIOTECH SI Ouirón Deveus University Hospital is a leading European institution in the field of
	mmunotherapy and target therapy for oncological patients. In particular, PANGAEA BIOTECH, S.L. has a major field
	pf investigation in the application of next generation technologies, such as multiplex colour code barcode technology,
	hat are relevant in the research that has been planned in this application. Main PI/co-supervisor: Miguel Molina. 3
	nonths.
	Main Supervisor: Prof Giancarlo Troncono (https://www.doconti.upipa.it/giancarlo.troncono)
Brief CV	Full Professor in Anatomic Pathology and Head of the Department of Public Health in School of Medicine University
	of Naples Federico II. His research interests include the development, validation, and quality assessment of a wide range of morpho-molecular techniques on cytopathologic specimens in the field of predictive pathology of solid
	tumors. He is the author of more than 300 papers in peer-reviewed journals (in particular: 1: Vigliar E, J Clin Pathol.
	2019;72:412-417. 2: Sgariglia J Clin Pathol. 2017;70:803-806. 3: Malapelle. Br J Cancer. 2017;116:802-810.). He
	serves on the editorial board of Pathobiology (associate editor), Cancer Cytopathology (associate editor) and Journal
Dublications	ot Molecular Pathology (Editor in Chief). He has supervised 8 PhDs.
Publications	- Malapelle U, et al. Reference standards for gene fusion molecular assays on cytological samples: an international
	- Malapelle U. et al. Development of a gene panel for next-generation sequencing of clinically relevant mutations in
	cell-free DNA from cancer patients. Br J Cancer. 2017 Mar 14;116(6):802-810.
	- De Luca C, Pepe F, Iaccarino A, et al. RNA-Based Assay for Next-Generation Sequencing of Clinically Relevant Gene
	Fusions in Non-Small Cell Lung Cancer. Cancers (Basel). 2021;13:139.
	worldwide ring trial study on improved cytological molecular reference specimens. Cancer Cytopathol. 2019;127:285-296
	- Malapelle U, et al. Consistency and reproducibility of next-generation sequencing and other multigene mutational
	assays: A worldwide ring trial study on quantitative cytological molecular reference specimens. Cancer Cytopathol.
	2017;125:615-626.
Projects	- "Nuovi Marcatori Molecolari nella Diagnostica Citologica Preoperatoria del Nodulo Tiroideo - TIRNET - Contributo
participation	ANNO 2021
	resistenti ai trattamenti (SATIN)"