BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

Innovative prostate biomarkers detection technique

Funded By	UNIVERSITA' DEGLI STUDI DI TORINO [P.iva/CF:02099550010]
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Context of the research activity	Prostate cancer is the most commonly solid neoplasm diagnosed in men. Approximately 300,000 new cases are diagnosed and more than 30,000 deaths recorded every year in the United States. The wide spectrum of severity of this condition encompasses both indolent cancer and rapidly evolving lethal disease. Unfortunately, to date the difference between indolent and aggressive cancers is not always recognized. Furthermore, response of cancer to current treatments varies according to the genetic features of the neoplasm, especially in advanced stages of disease. A thorough knowledge of all genetic alterations responsible for cancer progression would be invaluable. The evaluation of new biomarkers for diagnostic, therapeutic and prognostic purposes in this context is paramount and even modest improvements in patients care would have a dramatically positive impact on the global health burden.
	Several prostate cancer genetic biomarkers have been studied in recent years. First of all, the identification of germline and somatic pathogenetic variants of BRCA1 and BRCA2 genes are of special importance both for diagnostic (eg. family screening) prognostic and therapeutic (use of PARP-inhibitor agents) purposes. Also, androgen-receptor (AR) splice variants status (namely, AR-V7) could be highly informative for the correct sequencing of novel anti-androgen therapies, especially in the castration-resistant setting (abiraterone and enzalutamide). Finally, PSMA expression could become an important parameter when evaluating novel imaging techniques (eg. PSMA-PET) and possibly PSMA-guided surgery and

Objectives	radionuclide therapy. Despite recent guidelines (NCCN, AIOM 2021 etc.) recommend the execution of somatic and germline BRCA evaluation in many prostate cancer patients and despite the growing clinical need for precise therapeutic biomarkers, the access to these tests (which are mainly based on DNA sequencing, fluorescence in situ hybridisation (FISH) or immunochemistry) is still hampered by technical and economic issues, strongly limiting their availability. Moreover, somatic testing approach, usually requiring pathology specimens which are rarely available in the advanced disease, would benefit greatly from the so-called “liquid biopsy” approach, which detect mutations on circulating cancer cells using blood or urine samples. Increasing efforts are being made to overcome these problems. A promising and emerging technique for the identification of genetic mutations is based on surface-enhanced Raman spectroscopy (SERS). With this method, the genetic material (deriving from blood or urine samples) is absorbed (with no previous amplification) on gold nanoparticles and its electromagnetic spectrum is analysed using machine-learning developed algorithms, forming an “alphabet” of SERS fingerprints, eventually enabling to identify gene variants. Other approaches to liquid biopsies are based on next generation sequencing (nGS) techniques. After the development phase, a clinical validation of these promising approaches will be needed to assess diagnostic performance against the standard and to evaluate their impact on the disease management. The mission of this PhD programme is to design and establish a clinical assessment and validation of these emerging techniques, considering also the clinical and ethical implications, in order to help the development of a widely available, reliable and low-cost platform for the detection of prostate cancer biomarkers of clinical relevance. The focus will be on BRCA mutations, AR-V7 presence and PSMA expression. The research has several aims both at a candidate and at a clinical level. Candidate: To develop the profile of an expert in new prostate-cancer biomarkers implementation into clinical practice. To develop a cutting-edge clinical research curriculum To develop the theoretical and practical knowledge for translational research in prostate cancer field, facilitating the setting up of a multi-disciplinary network involving clinicians, bio-engineers, biologists and geneticists. Clinical: To identify the best existing standards for designing a validation study for new “liquid biopsy” strategies in prostate cancer (Raman spectroscopy, nGS), focusing on BRCA mutation, AR-V7 and PSMA expression. This should be done both at germline and somatic level, considering the various disease stages, tumour heterogeneity and mutation frequency. To design such validation study from a clinical perspective, starting the prospective sample collection that will allow a prompt comparison for

	emerging techniques. The collection of biologic fluids (such as blood, urine and saliva) and of tumour tissue (diagnostic biopsy, robotic prostatectomy, TURP, metastasis biopsy ecc) will be considered. To conduct such study for the cited biomarkers, also facing the ethical issues that will arise. To design and initiate a long-term cohort study for the validation of the prognostic and therapeutic significance of considered biomarkers. To evaluate biomarkers impact also on early therapeutic strategies of locally-advanced and oligo-metastatic disease, with particular reference to robotic radical prostatectomy, lymph-node dissection, metastasis-directed therapy, novel anti-androgen therapies. To help the setting-up of a multidisciplinary network for the clinical implementation of such techniques.

Skills and competencies for the development of the activity	Medical degree Ability to conduct clinical research and to write scientific articles Experience in multi-center clinical trials as Investigator and Study Coordinator Background in Prostate Cancer research Background in clinical research - at least twenty Pubmed publications with at least two first authorships English language and preferably another foreign language knowledge