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CASE REPORT

New antibody-based reagents for imaging and treatment of prostate cancer

This project is implemented through the CENTRAL EUROPE Programme co-financed by the ERDF

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Summary

The team propose to evaluate the potentiality of antibody fragments in targeting the glycoprotein Prostate Specific Membrane Antigen (PSMA). PSMA expression, already present in normal prostate epithelium, progressively increases from normal epithelium to organ confined prostate tumors, from primary to metastatic lesions and from hormone-dependent to hormone-independent tumors, and accordingly PSMA represents a good target antigen for prostate cancer.

Starting from proprietary anti-PSMA mouse antibodies: i) by molecular engineering, the research team converted the entire antibody into a single chain Fv (scFv) format; ii) by high up-date technologies, the research team selected starting from antibody libraries a completely human antibody fragment. These fragments, when analyzed in vitro, resulted to have adequate functionality and specificity and a good binding affinity. With the aim to develop new diagnostic and therapeutic tools for prostate cancer, the radio-labeled anti-PSMA fragments will be pre-clinically validated in animal models by conventional imaging and PET and the best radiopharmaceutical(s) assessed in a Phase I study in prostate cancer patients for tumour imaging and dosimeter.

Technology

An anti-PSMA antibody is already present on the market for prostate cancer imaging. This imaging agent (ProstaScint®) was obtained starting from the mouse monoclonal antibody 7E11-C5.3. This reagent is directed to cytoplasmic portion of PSMA detectable only on tumors upon cell destruction (necrosis).

Our anti-PSMA antibody fragments have the following advantages:

1. the binding to an extracellular PSMA region, well accessible in all types of metastasis;
2. a fragment format, that enables the production in prokaryotic systems (bacteria) and consequently a sensibly reduced cost of the reagent;
3. a small size that allows a better penetration in the tissues and a faster clearance from the blood compared to an entire antibody;
4. a low immunogenicity: in the case of the murine scFv, since it lacks the constant domains responsible of the majority of the Human Anti Mouse Antibody (HAMA) response; and in the case of the completely human fragment, due to its human origin.

Development stage

The innovation of the proposal concerns the use of new antibody fragments and the development of new radiopharmaceuticals. On the medium term (3-year period), the first generation reagent, i.e. the murine anti-PSMA scFv, whose fully characterization of specificity, productivity and stability was already concluded, will be used for preclinical and Phase I evaluation; on the long term (5-year period), the second

generation reagent, i.e. the new entirely human antibody fragment, following in vitro and in vivo validation, could enter in the clinics.

Market/Opportunity

Prostate carcinoma represents the second cause of male death due to neoplasia in industrialized countries. The incidence trend showed a steep increase all over Italy during the 1970-2005 estimation period and around 43.000 incident cases, 174.000 prevalent cases and 9.000 deaths were estimated in 2005 (data from Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy). There is a significant need, presently unmet, for an accurate diagnostic agent able to detect both location and extent of the prostate cancer. Information regarding the location of the cancer is critical when deciding local vs. systemic treatment options in the newly diagnosed prostate cancer patients. In addition, the most beneficial treatment for patients with occult recurrent disease is dependent on whether recurrence is local or systemic. An accurate staging tool would result in a more appropriate therapy.

IP

The murine scFv is under an Italian patent (n.T02008A000313).
International application n.: PCT/IB2009/005326.
Fondazione IRCCS Istituto Nazionale Tumori and University of Verona are co-owners of the patent.
Co-inventors are Dr Silvana Canevari and Dr Mariangela Figini from the Fondazione IRCCS Istituto Nazionale Tumori and Prof. Marco Colombatti and Dr Giulio Fracasso from the General Pathology Dept., University of Verona Medical School.

There are no constraints to the use of the patent.

Contact Details

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