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iRASP: a novel platform to design efficacious cancer targeted immunotherapies

Introduction

Since the approval of rituximab, antibody-based immunotherapies have dramatically changed the natural history of several cancer types. However, due to the paucity of viable tumor antigens discovered by the standard *target-first* approach, **only a few antibody-based drugs have entered into clinical use**. Furthermore, more than 50% of the available therapeutic antibodies target only five antigens, and consequently **no targeted immunotherapeutic option exists for the majority of cancer types**. Therefore, it has become of pivotal importance to design immunotherapies against novel tumor-associated antigens efficacious in halting currently untreatable tumors.

Medical Need

The *target-first* approach involves the discovery of tumor-specific antigens from high-throughput RNA- and DNA-sequencing data, or protein-based methodologies. Such strategy allows optimal tumor-antigen specificity due to dataset analyses, however the *in vivo* accessibility of tumor antigens remains uncertain and cannot be easily predicted. Additionally, such approach does not take into account a variety of post-translational modifications, which can either generate novel epitopes or mask the expected antigenicity.

Solution

Alternative to the *target-first* approach is the *antibody-first* strategy, which allows to unbiasedly identify tumor-specific antibodies, without prior knowledge of their target antigens. The inventors developed a unique platform, named iRASP (*in vivo* Recombinant Antibody-Screening Platform), that relies on antibody phage display libraries, *in vivo* screenings and next generation sequencing (NGS) to discover new therapeutic antibodies for cancer patients. It is a fast and cost-effectiveness platform that allows to *in vivo* isolate tumor-binding phage antibodies directly from tumor-bearing mice, and then shortlist the selected *in vivo* tumor-binders on the basis of the tumor specificity, thanks to a reliable and robust prioritization process. As a **proof of concept (funded by ERC PoC grant)**, a few independent iRASP-based candidates were isolated showing strong anti-tumor effect against both blood and solid untreatable tumors.

Application

iRASP platform can be tailored and applied to virtually **any tumor type**, starting from **different phage display libraries**, for the design of novel antibody-based immunotherapies (i.e naked therapeutic antibody, immuno-cytokine, bispecific antibody or CAR-T).

Advantages

New antibodies can be *in vivo* selected against patient-derived xenografts (PDXs) without prior knowledge of target antigen, and can be *in vitro* engineered to boost their **tumoricidal potential** or **tumor-targeting ability**. This approach provides the advantage of **immediately generating a viable tumor-specific antibody that can be directly tested *in vivo*.**

Opportunity

Istituto Europeo di Oncologia is seeking for partners interested in further exploiting our proprietary screening platform and developing the iRASP-based antibodies towards the clinical practice.

Principal Investigators

Pier Giuseppe Pelicci, MD PhD
IEO Research Director

- Prominent Scientist in Oncology
- Worldwide leader in Leukemia
- Greatly contributed seminal discoveries in cancer

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Drug Discovery & Immunotherapy Unit Director

- Over 15 years experience in discovery of targeted cancer drugs
- Expert in treatment and biology of haematological malignancies

References

Patent Application: PCT/EP2019/066217.

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