INTERVIEW

Proper delivery of cancer vaccines

The search for tumour immunotherapies has triggered huge investments, particularly for cancer checkpoint modulator candidates. Last February, Swiss-based Amal Therapeutics bagged a Series A financing involving the Boehringer Ingelheim Venture Fund and Hightech Gründerfonds as co-investors. The spin-out from the University of Geneva has developed a technology that triggers T cell-mediated immune responses against multiple tumour antigens by delivering multiple cancer antigen epitopes into antigen-presenting cells. EuroBiotechNews spoke with the company's co-founder Madiha Derouazi about Amal's platform and the company's goals.

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Dr. Derouazi, Amal means "hope" in Arabic. Why do you think your company's approach to delivering tumour antigens presented by $CD4^+$ and $CD8^+$ cells into antigen-presenting cells could prove more hopeful than other tumour vaccination approaches?

DEROUAZI: !
The immune system can recognise and to some extent eliminate tumour cells. However, this anti-tumour response is often of low amplitude and inefficient. Modulating the immune system to enhance anti-tumour immune response has become a promising therapeutic approach in oncology that can be used in combination with standard-of-care treatments. Building on the pre-clinical and clinical data accumulated during the past decade, Amal Therapeutics is developing an innovative approach allowing simultaneous activation of both helper and killer cells for different antigen specificities. This allows us to target a larger patient population and reduce the risk of having tumour cells escape the immune system.

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Could you outline the different steps of your company's tumour vaccination approach?

DEROUAZI: !
To initiate an anti-tumour immune response, either tumour-specific or tumour-associated antigens need to be delivered to antigen-presenting cells (APCs) such as dendritic cells (DCs). The DCs process the antigen and present their epitopes either to MHC class I restricted molecules – which are recognised by killer cells – or to MHC class II molecules, which are recognised by helper cells. The vaccine that we are developing is a recombinant protein. Protein vaccines primarily activate helper T cells, because the antigens are mostly processed and presented on MHC class II molecules. To improve MHC class I molecules, Amal Therapeutics is using a proprietary cell-penetrating peptide that promotes cross-presentation on MHC class I molecules and MHC class II presentation. Furthermore, we have designed a chimeric protein vaccine that is transported by the cell-penetrating peptide. This new recombinant vaccine simultaneously induces multi-epitopic killer and helper cells to function synergistically to counter tumour cells and promote efficient anti-tumour immunity. Helper cells are also involved in the maintenance of long-lasting cellular immunity, which is viewed as particularly important in the context of therapeu-

Amal Therapeutics' CEO Madiha Derouazi has been working on vector engineering and therapeutic cancer vaccines for nearly a decade. In the Laboratory of Tumour Immunology at the University of Geneva, she began developing different antigen delivery vectors, and designed and characterised the CPP-based multi-epitopic cancer vaccine that is currently being progressed by Amal Therapeutics.

tic cancer vaccines. Currently, we are finalising the technology platform by combining an appropriate adjuvant for the vaccine.

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What results did you see in mice using your approach?

DEROUAZI:
The vaccine promoted both MHC class I and II presentation *in vitro* as well as *in vivo*. We could monitor a good multi-epitopic immune response in mice for both killer cells and helper cells. We observed the establishment of a potent memory immunity after four vaccinations. The killer cells were then able to home in on the tumour site, and we observed a very potent protection against tumour development in a therapeutic setting (tumour implanted before vaccination began) in different tumour models in immune-competent mice.

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In which stage of preclinical development is your Zebra MultiE fusion protein currently, and when will you have all the data to apply for first-in-man studies?

DEROUAZI:
We are currently working on finalising our technology platform. We will then start to develop our lead vaccine candidate. Glioma is the cancer indication for which the therapeutic cancer vaccine will initially be developed. T lymphocytes can actively seek out neoplastic cells in the brain, and have the potential to safely eliminate specific tumour cells without damaging the surrounding healthy tissues. We are aiming to apply for first-in-man studies in 2016.

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Could you give our readers some background about the development of your platform technology and your spin-out from the University of Geneva?

DEROUAZI:
I have been working for nine years on the development of therapeutic cancer vaccines. At the University of Geneva, I started working on the cell-penetrating peptide-based approach that is now being move forward by Amal Therapeutics. The project has been supported through the Commission for Technology and Innovation (CTI) since 2012. Different grants allowed the project to be progressed within the university while consolidating the technology's IP position. Furthermore, different prize and foundation funding – including the support of the FIT (Fondation pour l'innovation technologique) and the Volkswirtschaft Stiftung, together with the CTI support – allowed us to bridge the gap between academia and start-up until the seed-financing round closed in February 2014.

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At what stage of development will you need a further financing round?

DEROUAZI:
We are planning to raise a series in early 2015 to progress our lead vaccine candidate through pre-clinical development.