AMAL Therapeutics
www.amaltherapeutics.com

Unique cancer vaccines target immunotherapy

Swiss-based AMAL Therapeutics is developing KISIMA, a unique protein-based immunization platform capable of producing single therapeutic vaccines for immunotherapy and beyond.

Therapeutic cancer vaccines have not lived up to their promise, eliciting less than robust immune responses or having an effect in few patients. Today, an indepth understanding of the root causes of late-stage vaccine trial failures has triggered a renewed interest in the field. A major finding to emerge is that two key players in the immune responses attack cancer cells: the helper and the killer T cell. Typically, antigens derived from extracellular proteins are presented on major histocompatibility complex (MHC) class II molecules and prompt a helper $CD4^+$ immune response, whereas antigens derived from cytosolic peptides are presented on MHC class I molecules and tend to induce a killer $CD8^+$ immune response. For potent anticancer immunity, both are needed and should ideally target several tumor antigens. Moreover, the T cells should also target antigens presented on different MHC molecules (alleles). If these criteria are met, such anticancer immunity should be applicable to broad patient populations while reducing the risk of immune escape. Unfortunately, many protein-based cancer vaccines result in the activation of mostly helper T cells, target only one or two antigens associated with few MHC molecules, and require the addition of a carefully chosen adjuvant to enhance their effect.

Enter AMAL Therapeutics, a Swiss biotech company that has developed KISIMA, a unique protein-based immunization platform. KISIMA (which means 'well' in Swahili) enables the production of a single therapeutic vaccine that comprises the three components necessary for a potent antitumor immune response: a cell-penetrating peptide (CPP) that transports a cargo across cell membranes; antigens (part of the cargo) that can be tailored to each indication; and a toll-like receptor peptide agonist that acts as an adjuvant (**Fig. 1**). The CPP behaves like a viral vector, delivering the antigens—whether large or small, self, neo or modified—into antigen-presenting cells, resulting in robust antitumor immunity owing to the simultaneous activation of both $CD4^+$ helper and $CD8^+$ killer T cells.

"Our outstanding vaccines increase antigen uptake, induce helper and cytotoxic T cells, and promote immunological memory. They are multiallelic, multiantigenic, self-adjuvanting, efficacious at low dose, allow for repeated vaccination, and do not elicit neutralizing antibodies," explained Madiha Derouazi, AMAL's CEO. "We are stimulating the immune system in a unique way with vaccines that target broad patient populations."

KISIMA vaccines have been validated in five different mouse tumor models with different antigenic cargos, eliciting $CD8^+$ T cell responses with a potency similar to adjuvanted vaccines and with a very good safety profile. The dose, route of injection, and vaccination schedule have also been optimized. Moreover, in a preliminary nonhuman primate study, the KISIMA vaccine primed both helper and killer T cell responses, demonstrating its capacity to overcome immune tolerance to tumor antigens—crucial for an efficacious anti-cancer immune response.

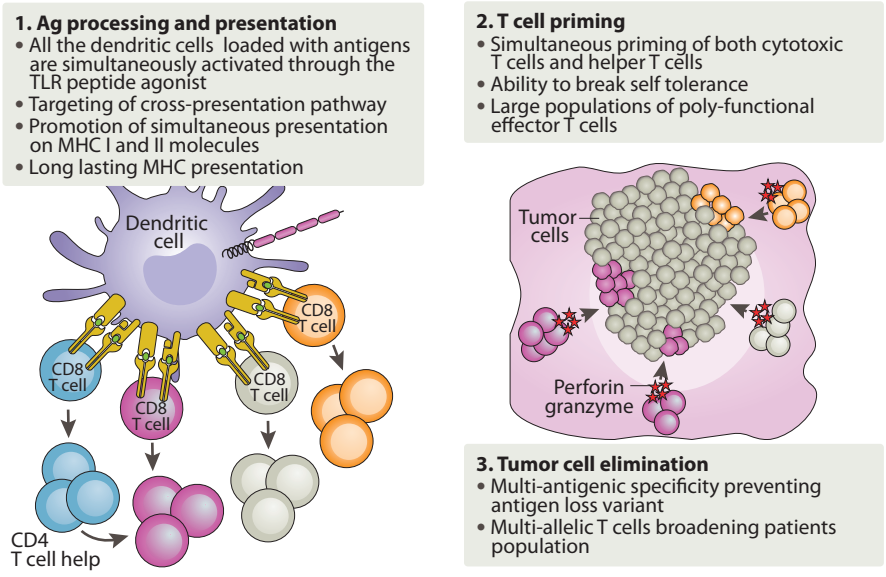

Fig. 1 | KISIMA, a unique protein-based immunization platform.

With successful anticancer immunity clearly requiring synergistic approaches, the use of KISIMA vaccines as a central component of combination therapy is set to considerably enhance the cancer immunotherapy field.

AMAL has compiled a strong data package for combination therapies (with ten molecules) that shows KISIMA immunization works synergistically with immune checkpoint inhibitors (ICIs), immune modulators, and viruses. "We have shown KISIMA immunization works in synergy with different ICIs in several tumor models, generating strong anticancer-specific immune responses," said Derouazi. "While checkpoint inhibitors reduce immunosuppressive effects, our vaccines boost proimmune effects, and can turn cold tumors [poorly infiltrated by T cells] into hot tumors [highly infiltrated by T cells]."

AMAL's lead product, ATP128, is currently being developed for stage IV colorectal cancer, a leading cause of cancer-related mortality and a significant market opportunity ($11 billion by 2025). Preclinical studies show that the use of this first-in-class cancer vaccine in combination with anti-PD1 treatment successfully controls tumor growth, and a first-in-human clinical trial of the combination will begin enrolling patients in the second half of 2019.

Partnering and licensing opportunities

The power and versatility of KISIMA can be harnessed to discover and develop therapeutic vaccines for a wide variety of indications, including infectious diseases. AMAL Therapeutics, with its design know-how and ability to develop a target into a hit in just 6 months, is offering licensing opportunities to fully exploit the potential of KISIMA—for example, for use in new indications, new treatment combinations, or for development as a synthetic platform for the delivery of neoantigens or modified epitopes.

Meanwhile, AMAL's aim is to advance the use of KISIMA for its current indications in oncology to phase 2 trials either in-house or through strategic partnerships, said Derouazi. "Our KISIMA technology results in the Swiss Army knife of cancer vaccines—a flexible and powerful way of extending therapeutic vaccination to many cancer indications, transforming the prospects of cancer patients."

contact
Madiha Derouazi, CEO
AMAL Therapeutics
Geneva, Switzerland
Tel: +41 22 379 46 83
Email: madiha.derouazi@amaltherapeutics.com