Chimeron Bio
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chimeron bio
An RNA Company

Amplifying the efficacy of RNA medicines

Chimeron Bio aims to transform RNA therapy with its novel nanoparticle technology by developing new vaccines and therapies based on self-amplifying RNA for the treatment of infectious diseases, oncology and rare genetic disorders.

Conventional RNA vaccines, such as those currently used to prevent severe SARS-CoV-2 infection, have problems with stability, require high dosing in the microgram range, and do not produce a durable response. Consequently, ultra-cold-chain storage and repeated dosing are required, and there are concerns about potential toxicity and side effects.

Solving these problems with a highly differentiated technology is Chimeron Bio, a preclinical biotech company that is developing the next generation of RNA drugs. Chimeron has developed a novel nanoparticle technology platform called ChaESAR (chimera-encased self-amplifying RNA) that harnesses the properties of self-amplifying RNA (saRNA) and synthetic genomics to engineer novel RNA therapeutics and vaccines for infectious and other diseases.

The ChaESAR platform

saRNA enables certain viruses to make multiple copies of their RNA genomes—and therefore encoded proteins—from a single RNA template. ChaESAR involves encapsulating saRNA that encodes a therapeutic gene of interest (such as an mRNA or an antigen) in a unique, proprietary non-lipid nanoparticle (NLNP) comprising viral glycoproteins. These ChaESAR particles are efficiently taken up by host cells and tissues, where the delivered RNA self-amplifies to make multiple copies of the gene (Fig. 1).

"With traditional mRNA technology, the mRNA delivered into a cell directly proceeds to protein synthesis. In contrast, saRNA delivered into a cell first self-amplifies, resulting in very high mRNA copy numbers, thereby achieving superior gene expression and an amplified protein response with a much lower amount of saRNA compared to other mRNA technologies," explained Thimmaiah Chendrimada, CSO of Chimeron Bio.

Chimeron's self-assembling glycoprotein-based nanoparticle technology can deliver a large cargo, including several genes or antigens of interest encapsulated in a single particle. This enables effective designs for broad-spectrum protection, while bypassing the need for technically difficult in vitro RNA synthesis. Furthermore, ChaESAR NLNP achieves activity in vivo in the picogram-to-nanogram RNA range and is stable at 4°C. The low-dose activity means the drug is likely to be less toxic, and the production mimics virus manufacturing workstreams and is therefore rapid and scalable.

Harnessing the targeted gene manipulation in cells enabled by ChaESAR, Chimeron is developing a compelling portfolio of innovative saRNA-based vaccines and therapeutics for infectious diseases, oncology and rare genetic disorders.

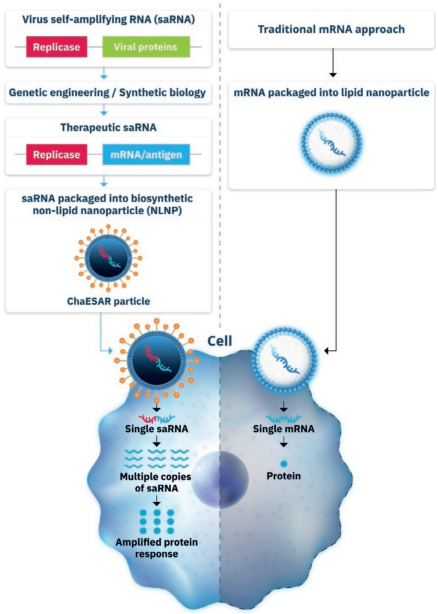

Fig. 1 | The working ChaESAR saRNA. mRNA delivered into a cell directly proceeds to protein synthesis (right). In contrast, saRNA delivered into a cell first self-amplifies, resulting in very high mRNA copy numbers, thereby achieving superior gene expression and an amplified protein response with a much lower amount of RNA compared to other mRNA technologies (left).

Targeting infectious diseases

The company's work on infectious disease includes both viral and non-viral diseases.

Chimeron has two programs directed for the prevention of COVID-19, including its lead candidate, CB-106, a vaccine that delivers the SARS-CoV-2 spike gene as an saRNA. Preclinical studies in rodents and rabbits show that nanogram quantities of RNA result in seroconversion without adjuvants, and with no toxicity observed to date. In March 2022, the US National Institute of Allergy and Infectious Diseases (NIAID) initiated a preclinical assessment of CB-106. Chimeron is also testing NLNPs containing saRNAs against several COVID variants.

The longer-term aim is to develop single-shot RNA vaccines that can deliver broad-spectrum protection against multiple variants or infectious agents. This could mean, for example, producing NLNPs for protection against several COVID variants, or combining saRNAs against influenza and COVID in the same particle, according to Chendrimada.

ChaESAR also has exciting potential for tackling malaria. Current malaria vaccination has only 36% efficacy because the single antigen it targets is relevant to only one point in the life cycle of the parasite. Taking advantage of the antigens identified for all life-cycle stages, Chimeron is planning to use ChaESAR to simultaneously deliver multiple antigens against the parasite, to successfully fight infection whatever phase the parasite is in.

"Our transformative platform enables the design of broad-spectrum vaccines that not only are low-dose and can, therefore, vaccinate many more people, but are also easy to manufacture, store and distribute via existing workstreams and networks," said Jolly Mazumdar, CEO of Chimeron Bio.

Broader pipeline

Additionally, Chimeron's pipeline includes four RNA therapeutics programs for treating solid tumors. Each program delivers multiple genes, and the designs range from an off-the-shelf personalized cancer vaccine (lead program CB-101) to cytokine delivery for modulating the tumor microenvironment. Preclinical data show that CB-101 inhibits tumor growth in vivo and demonstrates translational activity in human cancer cell lines.

The company also has a gene-therapy program, CB-151, for patients with alpha-1 antitrypsin deficiency (AATD), a rare genetic disease involving a toxic mutated form of AAT that can cause distinct lung and liver problems. Uniquely, CB-151 delivers both a healthy saRNA and a small interfering RNA to provide functional AAT and reduce mutant AAT, respectively, with in vitro data in liver cells confirming the feasibility of such a particle design.

Open for partnering

With such broad and translatable technology capabilities, Chimeron is open to a variety of collaborations. Potential partnerships include biopharma companies looking to develop novel vaccines with broad-spectrum protection against infectious diseases via the co-delivery of multiple antigens, for a heterologous prime-boost approach, or by leveraging the ChaESAR NLNP for low-dose durable expression of target genes or antigens.

"We are using our first-in-class platform to transform RNA therapy," said Mazumdar. "Our novel therapeutics and vaccines are highly differentiated and stand to improve patient access and outcomes worldwide."

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