APTAMERS FOR THE TREATMENT OF CONGENITAL AND ACQUIRED NEUTROPENIAS

Results achieved from researches from the CIBER rare diseases area offer an evidence of an efficient and safer therapy for the treatment of neutropenia (or diseases derived therefrom) and / or for the activation of myelopoiesis.

The necessity

Neutropenia is a dangerous and potentially fatal disease characterized by a lower-than-normal number of neutrophils in the circulation, either due to reduced production, high elimination or a storage problem. Neutropenia can be caused by multiple factors, such as chemotherapy (the most common cause), or genetic disorder as happen in dyskeratosis congenita (DC).

The solution

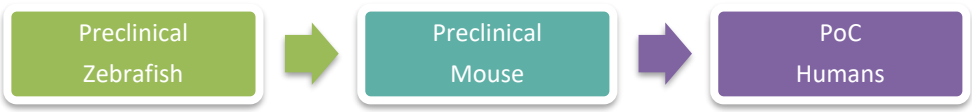
The group have designed several aptamers based in TERC (Telomerase RNA) sequence to activate myelopoiesis. Using these aptamers, we provided two potential therapeutic agents for DC and other neutropenic patients.

Innovative aspects

Aptamers are promising alternatives to antibodies and can be used as high affinity agents for the treatment of diseases. Therefore, several aptamers based on the TERC sequence were designed to investigate whether these small molecules could also increase myelopoiesis. Two aptamers were able to increase the number of neutrophils and macrophages, without affecting the number of erythrocytes in zebrafish models.

Aptamers function as the complete TERC molecule; that is, regulating the expression of the main myelopoiesis genes by binding to specific DNA sequences in the regulatory regions of these target genes and recruiting RNA Pol II to activate transcription. Using preclinical zebrafish models of diseases that occur with neutropenia, such as dyskeratosis congenita (DC, TERC deficiency) and poikiloderma disease with neutropenia (USB1 deficiency), the therapeutic effect of the developed aptamers was demonstrated, where the reversion was observed of neutropenias. Furthermore, treatment using the corresponding humanized aptamers also increased the expression of myelopoiesis regulatory genes and restored myelopoiesis in induced pluripotent cells (iPSCs) from healthy donor and DC patients with TERC mutations.

Stage of Development:
Developing pre-clinical studies required to apply for a Phase I/II clinical trial



Intellectual Property

Priority European patent application filed.
Suitable for international extension (PCT application).

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