

NEWS AND VIEWS

Clinical prospects for RNAi

Following rapidly from the explosion of interest in the therapeutic application of RNA interference, several compounds are now approaching clinical trials. Amongst the first to reach this hurdle is sirna-027, developed by Sirna Therapeutics (Boulder, CO, USA) as a treatment for age-related macular degeneration (AMD).

AMD is the most common cause of blindness in the western world for people over the age of 55. It results from damage to the macula, the part of the retina responsible for fine vision, though the periphery remains unaffected and so total blindness does not result. There are two clinically distinct forms – “Dry” AMD, which results from a gradual deterioration of retinal cells, and is responsible for 90% of cases, and “Wet” AMD, a more rapid deterioration of the retina which often develops in areas where dry AMD already exists.

There is no current cure for AMD, although laser surgery or photodynamic therapy may be used to slow the progression of Wet AMD. Sirna-027 is targeted to VEGFR-1, an endothelial growth factor receptor that stimulates the growth of new blood vessels, aiming to reduce the pathological angiogenesis associated with AMD. Application of sirna-027 is by direct injection into the eye, thereby negating many problems associated with delivery and stability in the body. Dr Roberto Guerciolini, Sirna's Senior Vice President and Chief Medical Officer of Sirna technology, commented, that sirna-027 has been chemically modified, and “has shown a significantly improved pharmacokinetic profile in pre-clinical studies compared to unmodified siRNAs”.

Phase I clinical findings have so far proved positive. Of 14 patients with the blindness-causing Wet AMD, deterioration in visual acuity has been halted and a dose-dependent improvement (100-800µg) in reading tests observed. Additionally, thickening of the retina has been reduced in six of seven patients examined using optical coherence tomography.

Though buoyed by the initial success of sirna-027, many researchers will also remember the promise of early antisense therapeutics, such as Fomivirsen (Vitravene™), the first antisense therapeutic to reach the market, and by no coincidence also targeting a retinal disease. Yoon Sang Cho-Chung of the NIH's Therapeutic Oligonucleotide Interest Group believes, “Systemic treatment, especially for targeting tumours, is still quite far away.” As with antisense therapeutics, stability and delivery still remain significant obstacles to be overcome, though due to the similarities between RNAi and antisense approaches, 25 years experience in optimising antisense reagents should significantly enhance the progress of RNAi-based therapeutics.

REFERENCES

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