Transposons in ophthalmology

Dear Editor,

Transposons (Ts) or “jumping genes” which change position in the genome, can be as a tiny as 0.7 kilobases (kb) or as large as 500 kbp. Until very recently they were regarded as inactive genetic material (fossil). At present it is known that, being mutagenic, they are an essential factor in some diseases. The “jumps” by Ts are able to activate and deactivate genes. The majority of Ts are inactive but a minority have the capacity to become activated, and their expression is potentially harmful. Although they only account for 0.27% of diseases associated to mutations, they relate to severe neurodegenerative processes (frontotemporal lobe degeneration, amiotrophic lateral sclerosis, schizophrenia), hemophilia A and B, severe combined immunodeficiency, Duchenne’s disease, predisposition to cancer and neurofibromatosis. It seems difficult to understand how genes, the biological database, can move and jump from one chromosome to another and modify DNA, dragging an encoding gene from one chromosome to another or breaking it in half. In this action, the transposase enzyme which joins the transposon (T) to specific DNA sites plays an essential role. Any excessive mobility (transposition) could be due to hereditary causes but could also be caused by the environment (epigenetic origin). Why are Ts important in ophthalmology and why should we be aware of their existence? Firstly because they are associated to purely ophthalmological and extraculcular diseases with ophthalmological expressions (von Hippel-Lindau disease, choroideremia, diseases linked to chromosome X, recessive autosomic cataract [lop11], albinism. The deficiency of DICER 1 in nonvascular ARMD produces toxicity due to Ts overexpression [ALOR ARN]3), and secondly because they are a tool used in gene therapy, mainly in retinal diseases. Monogenic diseases, i.e., those due to the mutation of a single gene, could be the cause of rare hereditary diseases (hereditary retinal dystrophy). However, the most prevalent human diseases like cancer, mental disorders, diabetic retinopathy, glaucoma or ARMD have much more subtle genetic components. Gene therapy has gone from the lab to the clinic, utilizing viral and non-viral vectors (vehicles for carrying the gene to the target cell) but with certain limitations (dissemination, immune response, mutagenesis, low efficacy). These limitations can be overcome using Ts as a non-viral gene-releasing system with maintained efficacy in transgenic expression due to permanent insertion in the genome of the host cells. For example, the objective in ARMD would be to replace degenerated RPE cells by genetically modified cells utilizing a T as a gene-releasing system that continually produces the pigment epithelium derived factor which is essential to maintain the avascularity of the subretinal space, inhibiting neovascularization and in addition being neuroprotective. Ts are also used as gene transfer vectors that combine the efficacy of the viral vectors with safety in order to maintain transgene expression. The literature includes examples illustrating how Ts can be used as a reservoir of genetic innovation. This type of innovation includes the creation of new encoding or non-encoding genes with beneficial functions for cells. This represents a significant development for genetics and therapies which utilize Ts as tools.

REFERENCES


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Please cite this article as: Asensio-Sánchez VM. Transposones en oftalmología. Arch Soc Esp Oftalmol. 2015;90:349–349.