Chapter 17
Web Text Box 5

Lamins, disease and ageing

At the latest count, 85 human diseases are known to result from mutations in intermediate filament proteins. Amongst the most surprising findings is the link between lamins and ageing. There are two rare human diseases that result in accelerated ageing (progeria): Hutchinson-Gilford Progeria Syndrome (HGPS) and Werner's syndrome. In HGPS, children commonly die between the ages of 13-20 of diseases more typically associated with advanced age such as atherosclerosis and cardiovascular disease. HGPS patients produce a splice variant of lamin A (one of the three lamins that together form the nuclear lamina, see book page 47) called either LAΔ50 (because the last 50 amino acids are missing) or progerin. Progerin is in fact expressed as part of the normal ageing process but it is not normally seen until advanced age. Instead of having smooth, even contours, nuclei in cells cultured from HGPS patients appear highly distorted. Although we do not yet know why disruption of nuclear envelope should result in the advancement of ageing, the answer probably lies in the control of gene expression. Chromosomes occupy precise territories within the nucleus, in part at least due to their interaction with the inner face of the nuclear envelope (where lamin A is located). Disruption of this arrangement may result in genes that are normally activated late becoming switched on at the start of development. It should be stressed that ageing is a complex process that involves many genes. However, it looks increasingly likely that the correct processing of lamin A plays an important role.