

STRESS, MUTATIONS AND AGING

Professor Tom Kirkwood

Henry Wellcome Laboratory for Biogerontology, Institute for Aging and Health, University of Newcastle upon Tyne, UK

As predicted by the disposable soma theory of aging, evidence from many lines of research confirms that senescence is a process of gradual accumulation of damage in cells and tissues of the body, leading eventually to frailty and increased risk from a spectrum of age-associated diseases. Multiple kinds of stress-induced damage affect cells, ranging from mutations in DNA to oxidative attack on proteins. Some of our recent work has shown how this damage impairs the function of tissue stem cells – specifically stem cells of intestinal epithelium – as ageing proceeds. The key to understanding the factors that regulate aging and longevity is to be found in the network of cell maintenance systems that slow the accumulation of damage. For example, long-lived species carried out repair better than short-lived species and are endowed with greater capacity to withstand stressors. A major challenge is therefore to understand how the diverse mechanisms which make up this network interact with each other. Using mathematical and computer modeling of molecular mechanisms of aging, we are developing a Biology of Aging e-Science Integration and Simulation system (BASIS) to support the development of an integrated understanding of the underlying cell and molecular mechanisms of age-related frailty and disease.