Ageing is the main risk factor for cardiovascular diseases, including atherosclerosis, vascular calcification, cardiac arrhythmias, myocardial infarction and stroke. These disorders, which nowadays represent the main cause of morbimortality in developed countries, are estimated to become the main cause of death world-wide within two decades. Hutchinson-Gilford progeria syndrome (HGPS) is a rare premature aging disorder (1 in 4.8 million newborns) that recapitulates some biological and physical aspects of physiological ageing, including atherosclerosis, calcification of aorta and aortic valves and electrocardiographic alterations. Patients die at an average age of 13 years, predominantly from myocardial infarction or stroke. Most HGPS patients are heterozygous for a silent dominant mutation in the \textit{LMNA} gene (1824C>T; p.G608G) that causes the expression of progerin, a prelamin A mutant lacking that retains a carboxy-terminal toxic farnesyl modification. Defects in the zinc metalloprotease ZMPSTE24/FACE-1 which cause the accumulation of farnesylated prelamin A also accelerate ageing.

We investigate the mechanisms underlying cardiovascular alterations in progeria using cellular and mouse progeroid models, including \textit{Lmna}^{G608G} knock-in mice, which express farnesylated progerin, \textit{Zmpste24}−/−null mice, which express farnesylated prelamin A, and cells from these mutant mice and HGPS patients. Our studies are identifying mechanisms through which progerin and prelamin A promote atherosclerosis, electrocardiographic alterations and vascular calcification. Remarkably, recent studies demonstrate that both progerin and prelamin A are expressed in aging cells and tissues of non-HGPS subjects, thus suggesting their contribution to organismal aging in the general population.