Endonuclease G and AIF, both mitochondrial nucleases, have been suggested to play a crucial role in genuine mitochondrial function but also in apoptosis during a plethora of degenerative disorders such as noise induced hearing loss, neurodegeneration and muscle degeneration during ageing.

We describe the yeast and fly orthologues of Endo G (Nuc1p and EndoG) whose overexpression triggers apoptotic cell death. Nuc1p displays mitochondrially-nuclear localization and induces apoptosis in yeast independently of caspases or AIF. Instead, we found other biochemical interactors necessary for cell death upon Nuc1 overexpression. We thus picture for the first time a pathway for EndoG mediated death.

Yeasts mutated in the ER residing calcium pump PMR1 (whose mutation in mammalian cells is responsible for hereditary Haily-Haily disease) die during chronological ageing in a caspase-independent but Aif1-dependent fashion.

We can dissect the lethal and vital functions of AIF as well as caspase-dependent and -independent pathways in a single yeast mutant.