Oxidative stress in cells with extra centrosomes drives non-cell autonomous invasion

The centrosome is the main microtubule-organising centre in animal cells; important to assemble a bipolar mitotic spindle ensuring proper chromosome segregation and genomic stability. Centrosomal abnormalities, in particular centrosome amplification, are recurrent features of human tumours. Enforced centrosome amplification in vivo plays a role in tumour initiation and progression. However, centrosome amplification occurs only in a subset of cancer cells and thus, partly due to this heterogeneity, the contribution of centrosome amplification to tumours is unknown. Here, we show that supernumerary centrosomes induce a paracrine-signalling axis via the secretion of proteins, including interleukin 8 (IL8), which leads to non-cell autonomous invasion in 3D mammary organoids and zebrafish models. This extra centrosomes-associated secretory phenotype (ECASP) promotes invasion of human mammary cells via HER2 signalling activation. Further, we demonstrate that centrosome amplification induces an early oxidative stress response via increased NOX-generated reactive oxygen species (ROS), which in turn mediates secretion of pro-invasive factors. The discovery that cells with extra centrosomes can manipulate the surrounding cells highlights unforeseen and far-reaching consequences of these abnormalities in cancer.