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Inflammation, senescence and cancer: interweaving microRNA, inflammatory cytokines and p53 networks

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The p53 pathway is an intrinsic monitor and response pathway of telomeric attrition involved in cellular aging and senescence. Cellular senescence is tumor suppressive that can be activated by p53 in cancer cells. We are studying the molecular mechanisms of cellular senescence in normal and malignant human cells and the role of the telometric multiprotein complex, shelterin, that includes TRF2 and POT1 [1-3]. Our ongoing studies have revealed that p53 and its endogenous isoforms regulate both specific microRNAs and TRF2 expression as mechanisms of replicative senescence. In addition, POT1 isoforms are functionally diverse in both maintaining telomeric integrity and preventing p53-dependent senescence induced by telomeric shortening. A switch in the expression patterns of p53 isoforms, Δ133Np53 and p53 beta, is also associated with the transition of benign to malignant human cancers.

Chronic inflammation and deregulation of microRNAs have roles in human carcinogenesis [4-7]. In addition to our mechanistic and genetic studies, we are investigating the expression of microRNAs and inflammatory genes as cancer biomarkers of diagnosis, prognosis, and therapeutic outcome [8-11]. We are especially interested in developing prognostic classifiers of early stage cancer.

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