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Mammographic density, circadian clocks and breast cancer

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Very little is known about the mechanisms that start breast cancer. High mammographic density is the strongest risk factor known, and we discovered that high density is linked with reorganization and stiffening of the stromal extracellular matrix. Recently we showed that breast tissue has strong circadian (24-hourly) rhythms, with over 600 genes being expressed in daily 24 hour cycles. Altered circadian rhythms are known to contribute to breast cancer, but the underlying mechanisms are not clear. We found that the breast circadian clock is under the control of the cellular microenvironment, and that stiffness of stromal tissue determines the amplitude of breast clocks via integrins and a Rho-mediated control on intracellular signalling. We have recently demonstrated that early human breast cancers are surrounded by biophysically stiffer stroma than normal tissue from the same patients, and that circadian clocks within cancerous breast epithelium are hugely disrupted.