**Plasticity of melanoma cell stiffness increases with tumor malignant progression**

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**Background:** Elastic properties of carcinoma cells vary during tumor progression. It is unknown whether cell elastic properties vary similarly during malignant progression of melanoma, a tumor derived from melanocytes which are cells of neuroectodermal origin. Melanoma progresses from non-invasive Radial Growth Phase (RGP) to Vertical Growth Phase (VGP) and to metastatic tumors.

**Objective:** To analyze by Atomic Force microscopy the elastic properties of normal melanocytes (NHEM), RGP (SBC12), VGP (WM115) and metastatic (WM239A) melanoma cells in relation to adhesion to Extracellular Matrix (ECM) proteins, cell morphology and motility.

**RESULTS**

![Graph](image)

**Fig 1.** Melanoma elasticity is affected by cell malignancy, substrate chemistry and cell morphology. Young's modulus (A) and images (B) of NHEM and melanoma cells in different adhesion conditions.

Melanoma cell elasticity is influenced by:

- the degree of malignancy. Cell stiffness decreases in initial stages of malignant transformation (from NHEM to RGP, to VGP) but increases as cells acquire metastatic properties.
- the adhesion substrate, cell morphology, cytoskeleton organization and incubation time. VGP and metastatic melanoma cells show an increased ability to modulate stiffness in response to ECM-mediated adhesion and spreading, whereas only minor changes in stiffness were seen for melanocytes and RGP melanoma cells.

![Graph](image)

**Fig 2.** Malignancy and motility properties of NHEM and melanoma cells. A) Colony formation in soft agar. B) Colony formation in lungs of mice upon tail vein injection. C) Transwell migration towards Fetal Calf Serum.

- In vitro and in vivo colony formation of melanoma cells is increased with degree of malignancy: met>VGP>RGP>NHEM
- Elasticity of melanoma cells (VGP>RGP>NHEM>met) is not correlated with in vitro motility.
- TGF decreases melanoma cell motility but does not affect elasticity

![Graph](image)

**Fig 3.** Modulation of the motility properties of melanoma cells are not accompanied by changes in cell elasticity. Transwell migration (A) and Young’s modulus (B) of WM239A upon TGFβ stimulation.

**CONCLUSIONS**

- Elasticity is a dynamic property of melanoma cells.
- Increased plasticity (i.e. the ability to adjust elasticity to variable external conditions) of melanoma cells rather than decreased stiffness (as observed for carcinoma cells) is a marker of malignancy.
- Caution needed in the use of Atomic Force microscopy analysis for diagnostic purposes in melanoma patients.

![Diagram](image)

**Fig 4.** Model of melanoma metastasis formation (a-c) requiring dynamic elastic properties (d), manifested in the acquisition of a high degree of cell plasticity as malignancy progresses.

Table 1. Young’s modulus values for NHEM and melanoma cells in different adhesion conditions. *p<0.05, **p<0.01, ns: not significant.