AFM analysis of P-cadherin/SFK mechanotransduction signalling in breast cancer cells

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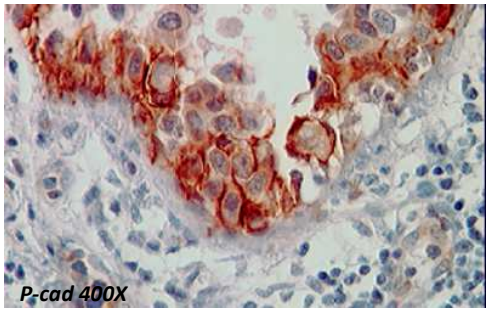
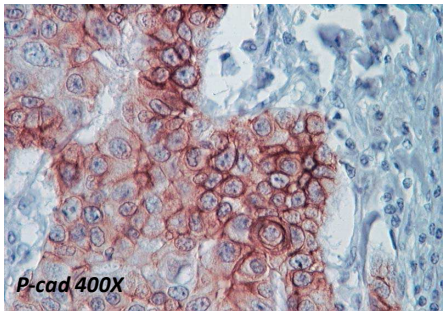
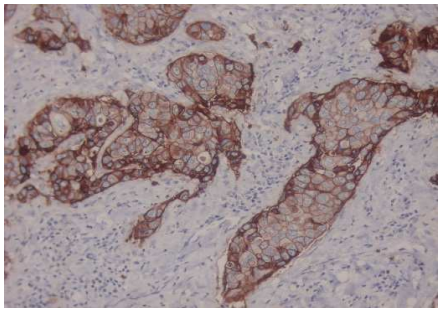
P-CADHERIN: A POOR PROGNOSIS PREDICTOR IN BREAST CANCER

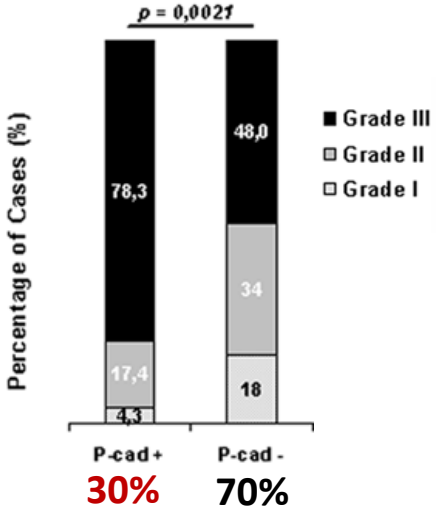




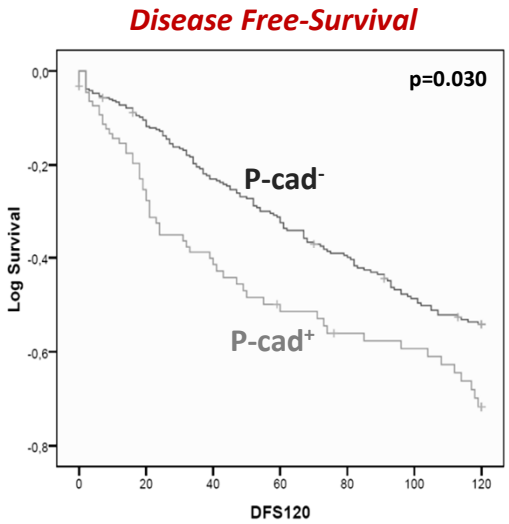


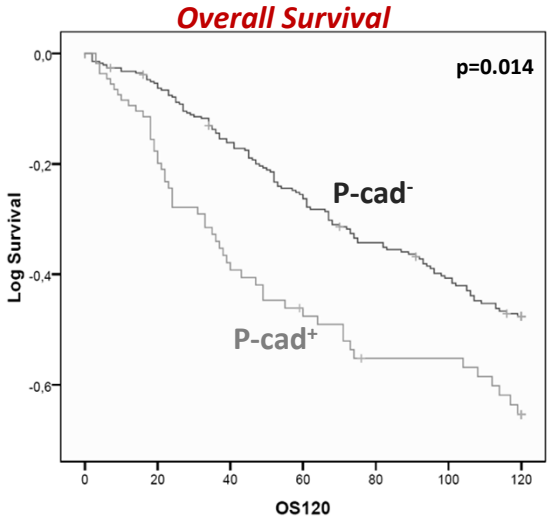
Strong membranous and cytoplasmic expression of P-cadherin in a high-grade invasive breast carcinoma.

P-cadherin expression and tumor histologic grade



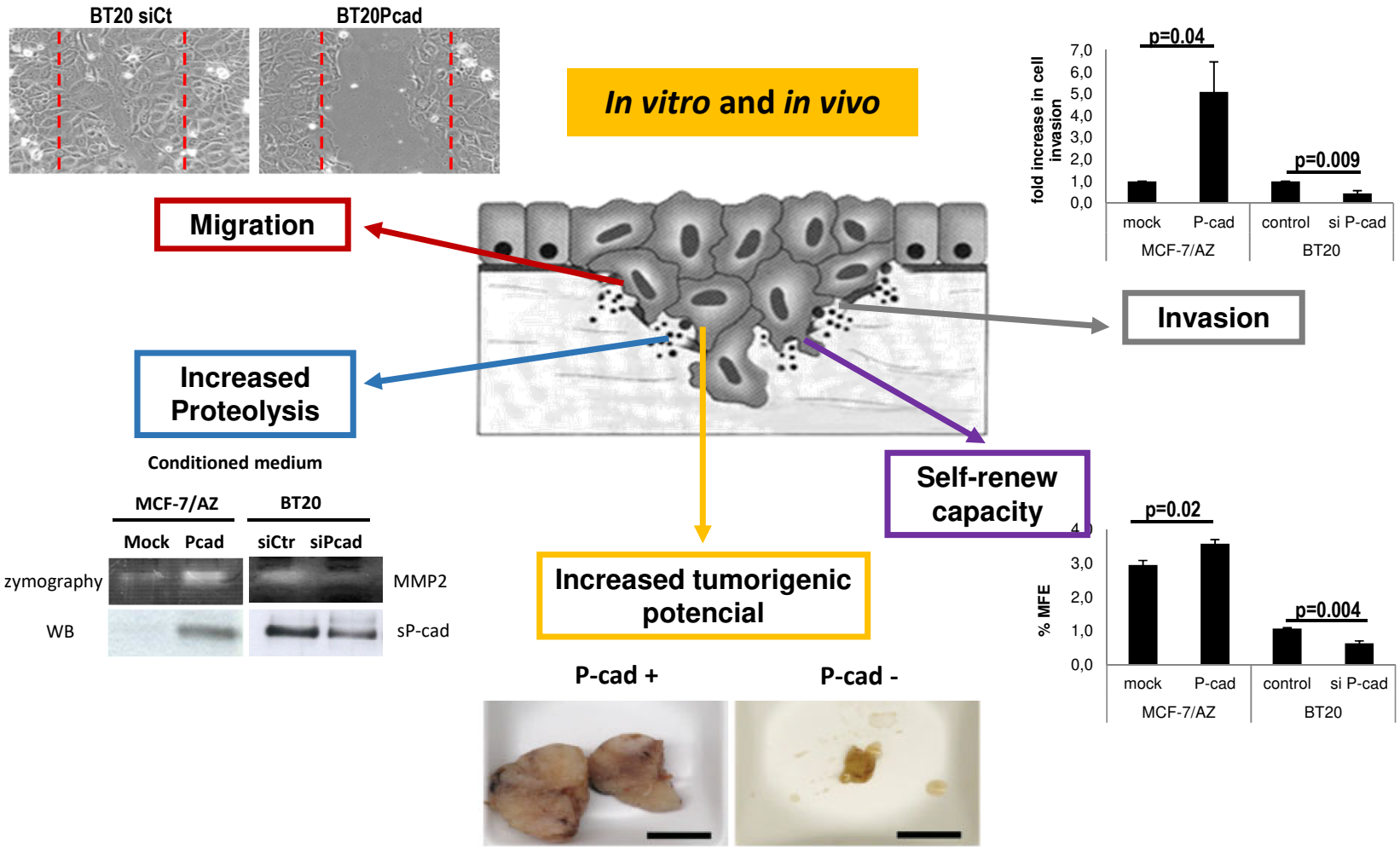
Patients with P-cad^{+} tumors *vs.* patients with P-cad^{-} tumors





Paredes *et al.* Virchow Arch 2002; Paredes *et al.* Cancer Res 2004; Paredes *et al.* Clin Cancer Res 2005; Paredes *et al.* Breast Cancer Res 2007

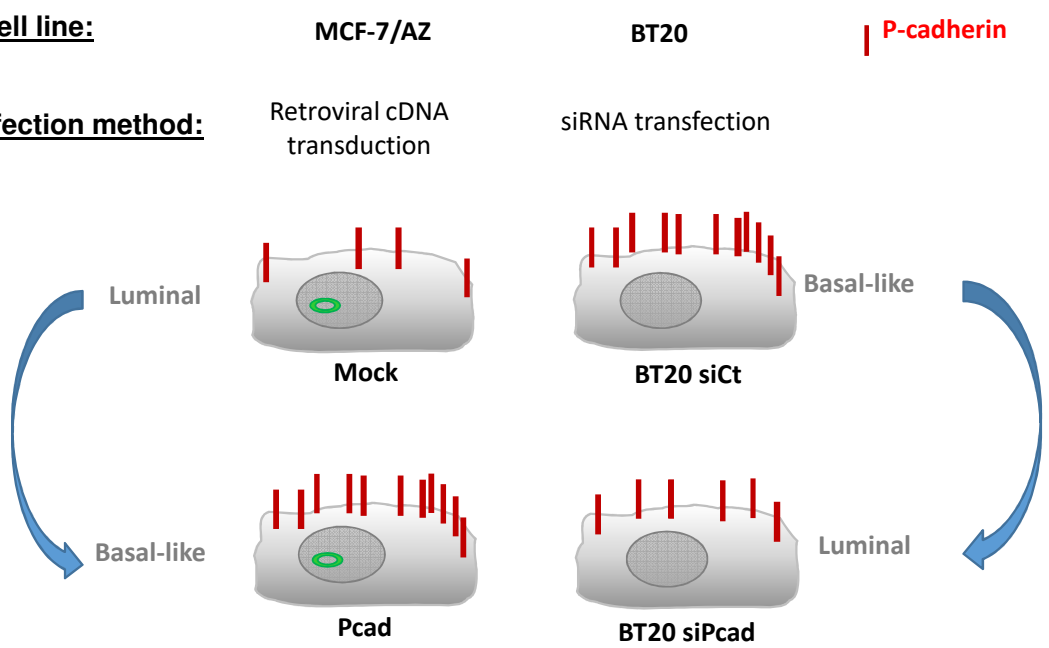
P-CADHERIN ROLE IN BREAST CANCER PROGRESSION

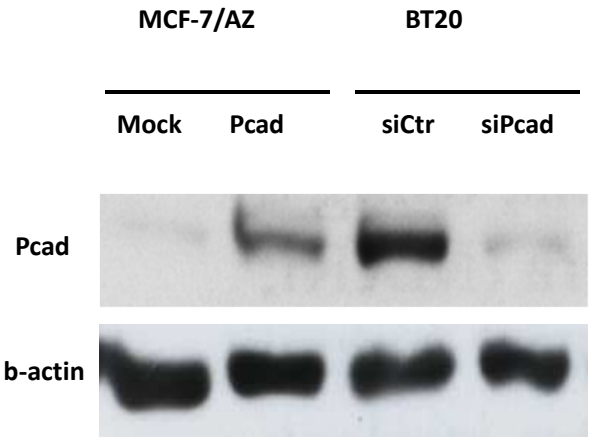


Ribeiro AS *et al.*, Oncogene 2009; Vieira AF *et al.*, Stem Cell 2012; Ribeiro AS *et al.*, J Pathol 2013

CELL MODEL

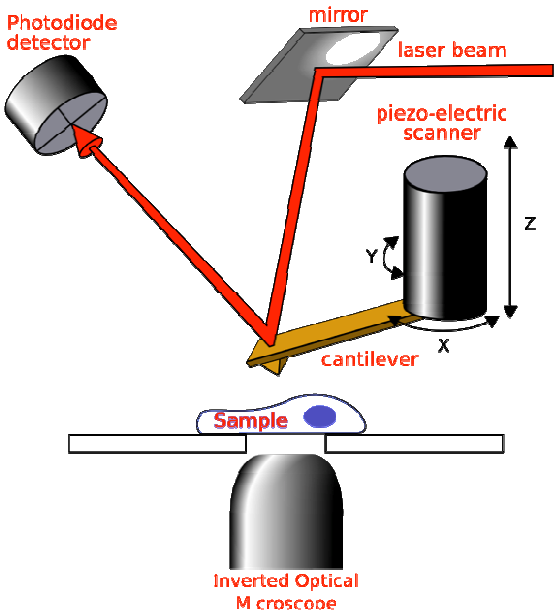
In vitro model of induction of a basal-like breast cancer phenotype





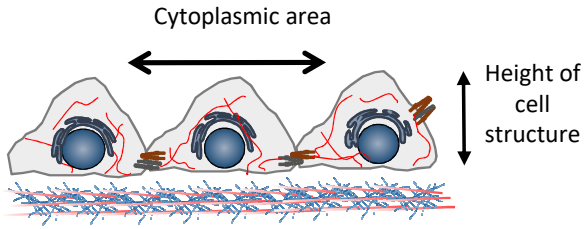
METHODS

ATOMIC FORCE MICROSCOPY

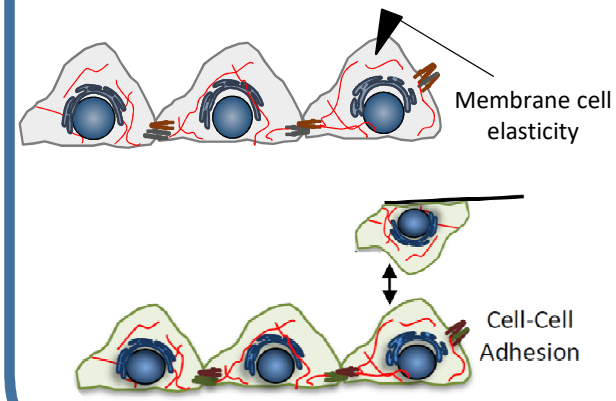


AFM

AFM Image analysis



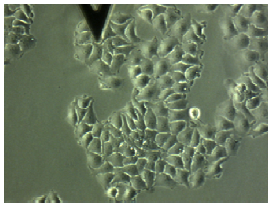
AFM Force Spectroscopy



RESULTS

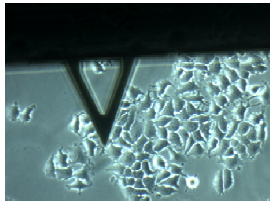
P-cadherin overexpression promotes morphological and biomechanical changes associated with a more invasive phenotype.

MCF-7/AZ.MOCK



(magnification 16x)

MCF-7/AZ.PCAD



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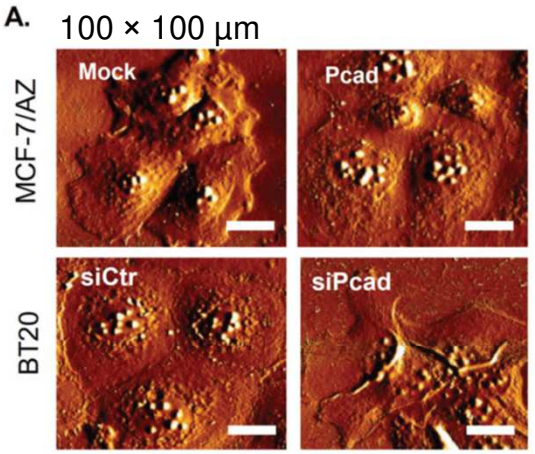
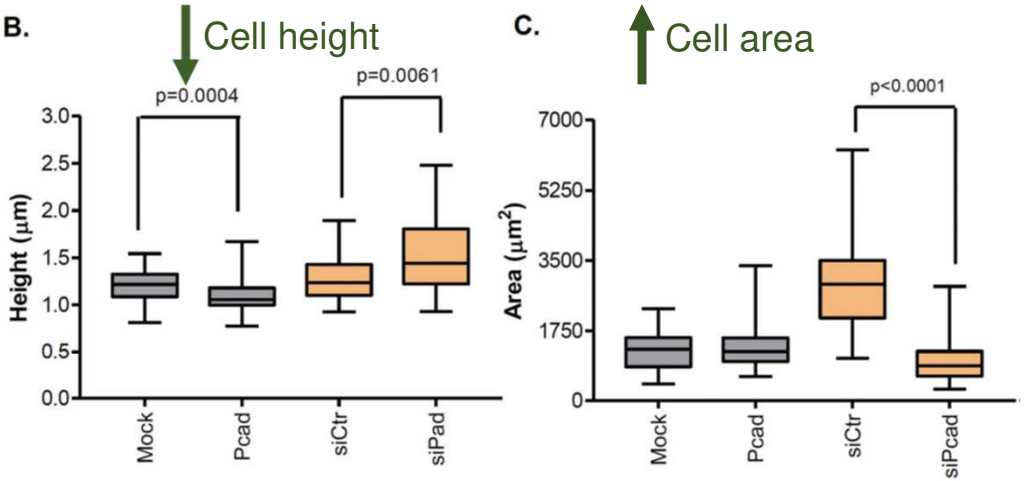
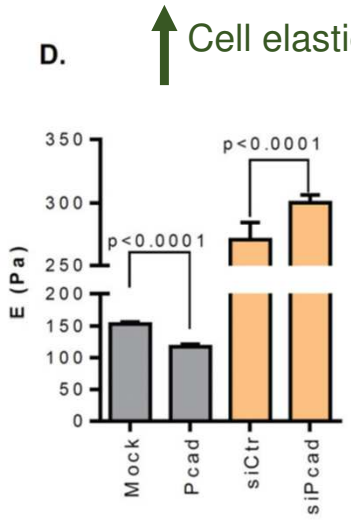
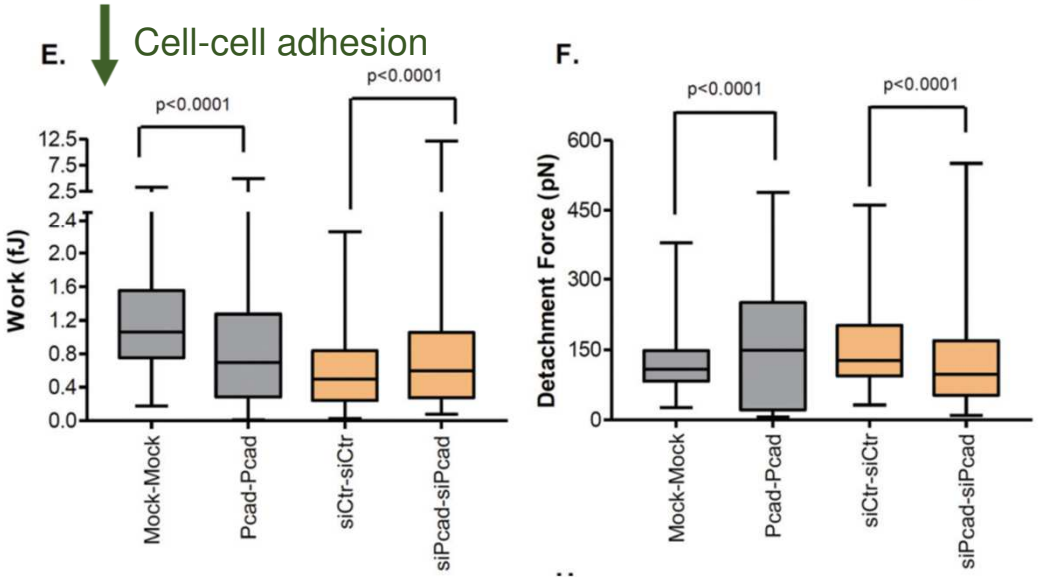








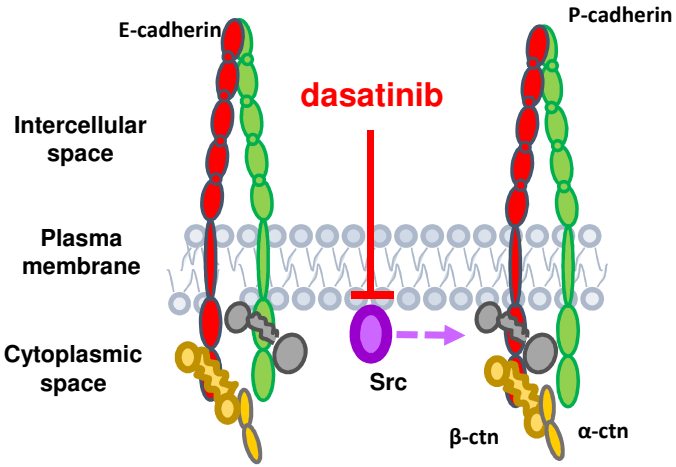
LEGEND

MCF-7/AZ

BT20

RESULTS

P-CADHERIN OVEREXPRESSING CELLS SHOW Src FAMILY KINASE (SFK) ACTIVATION

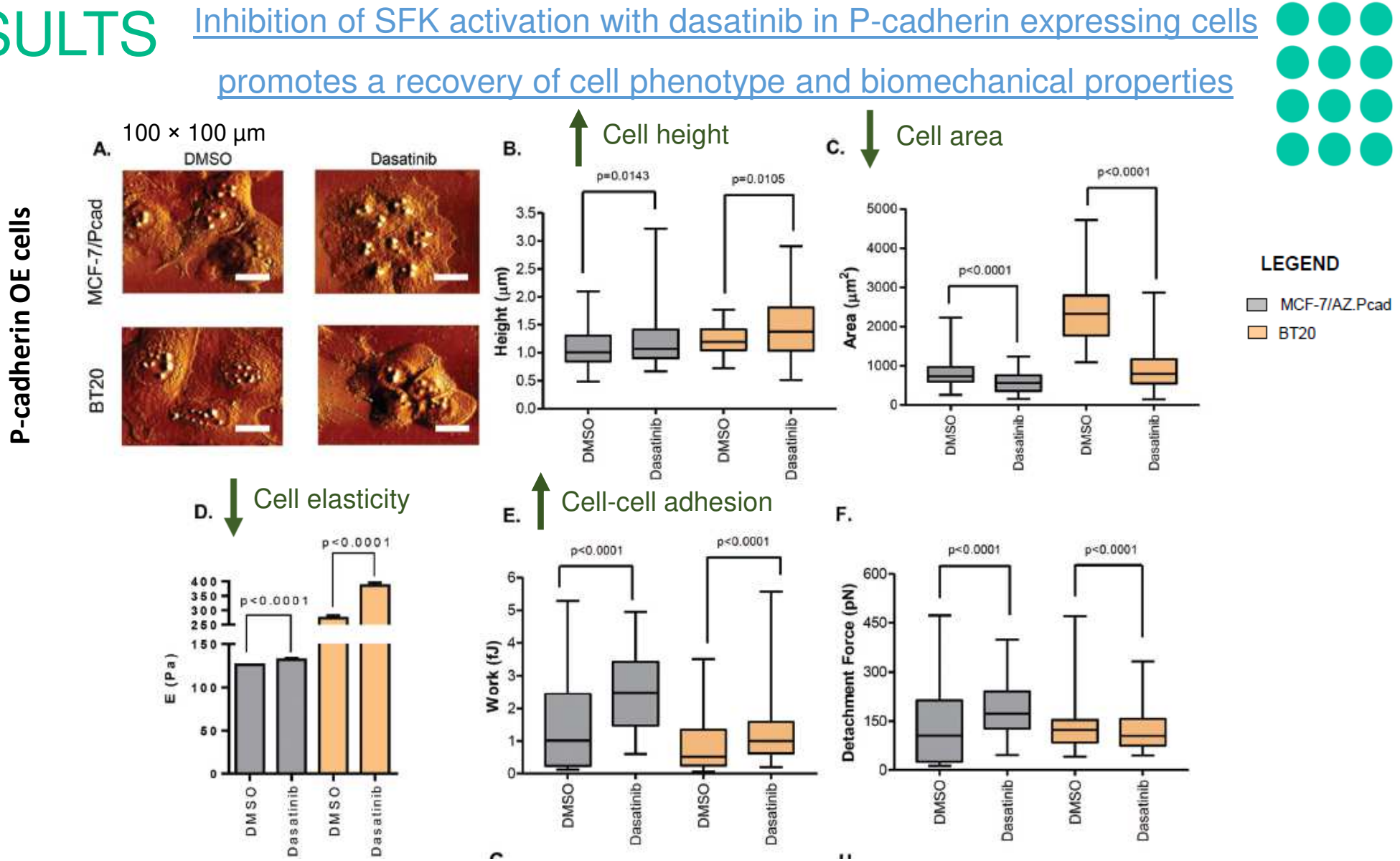


Dasatinib is an oral tyrosine kinase inhibitor that potently inhibits SFKs

Dasatinib is approved for treatment of imatinib-resistant and imatinib-intolerant chronic myeloid leukemia and Philadelphia chromosome-positive acute lymphoblastic leukemia.

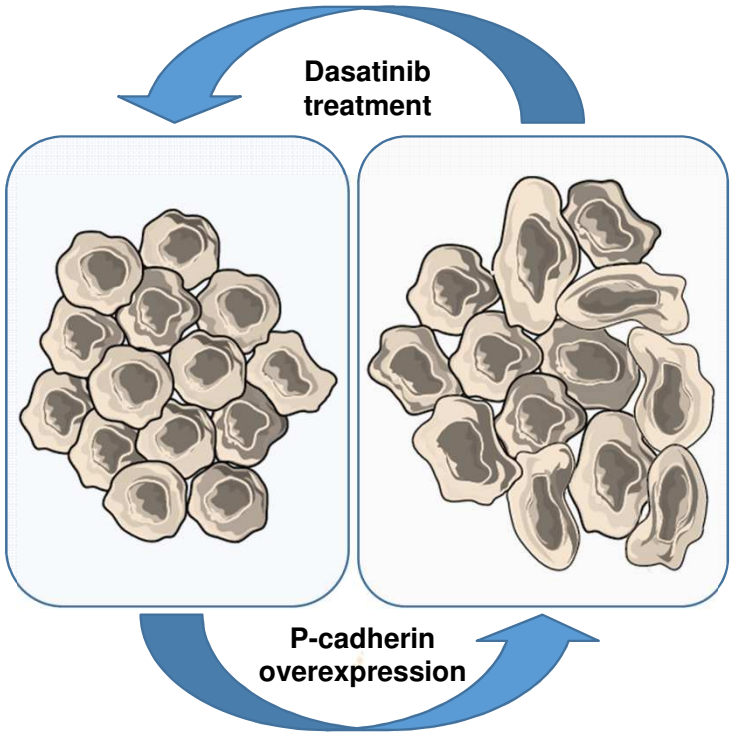
RESULTS

Inhibition of SFK activation with dasatinib in P-cadherin expressing cells promotes a recovery of cell phenotype and biomechanical properties



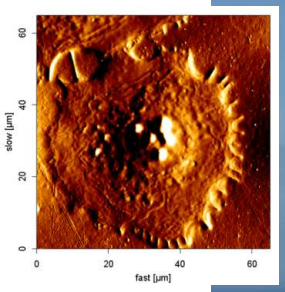
CONCLUSIONS

AFM



- Decreased cell height
- Increased cell area
- Higher elasticity
- Decreased cell-cell adhesion

ACKNOWLEDGMENTS



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