

Abstract Submitted  
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**Multicellular contractility contributes to the emergence of mesothelioma nodules.**<sup>1</sup> ANDRAS CZIROK, University of Kansas Medical Center — Malignant pleural mesothelioma (MPM) nodules arise from the mesothelial lining of the pleural cavity by a poorly understood mechanism. We demonstrate that macroscopic multicellular aggregates, reminiscent of the MPM nodules found in patients, develop when MPM cell lines are cultured at high cell densities for several weeks. Surprisingly, the nodule-like aggregates do not arise by excessive local cell proliferation, but by myosin II-driven cell contractility. Contractile nodules contain prominent actin cables that can span several cells. Several features of the in vitro MPM nodule development can be explained by a computational model that assumes uniform and steady intercellular contractile forces within a monolayer of cells, and a mechanical load-dependent lifetime of cell-cell contacts. The model behaves as a self-tensioned Maxwell fluid and exhibits an instability that leads to pattern formation. Altogether, our findings suggest that inhibition of the actomyosin system may provide a hitherto not utilized therapeutic approach to affect MPM growth.

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