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## **Tumor cells forming vasculogenic mimicry patterns in three-dimensional melanoma cultures have increased resistance against cytotoxic agents and express stem cell marker CD271**

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Vasculogenic mimicry (VM) patterns are present in numerous malignant tumor types, represent the formation of perfusion pathways by tumor cells, and their presence in tumors is associated with adverse outcome. Mechanisms by which VM may contribute to adverse outcome are not well understood. Previous observations in our laboratory indicated that VM-forming tumor cells in three-dimensional (3D) uveal melanoma cultures have increased resistance against oncolytic virotherapy. To determine whether VM-forming tumor cell subpopulations also have increased resistance against cytotoxic drugs, traditional two-dimensional (2D) and extracellular matrix (Matrigel)-containing 3D cultures of C918 uveal melanoma cells were established and exposed to cisplatin or cadmium chloride. We found that VM-forming tumor cells demonstrated prolonged survival relative to other tumor cell subpopulations in 3D cultures and to cells grown in 2D. To explore the possibility that the increased therapy resistance of VM-forming tumor cells is due to a cancer stem cell phenotype, the expression of cancer stem cell marker CD271 was determined in 2D and 3D uveal melanoma cultures by fluorescent immunocytochemistry. We found that the VM-forming tumor cell subpopulation in 3D cultures expressed CD271. In contrast, cells grown in 2D cultures and tumor cell subpopulations not participating in VM formation in 3D cultures were negative for CD271. These findings suggest that increased drug resistance is a mechanism by which VM-forming tumor cells contribute to adverse outcome. Our findings also suggest that VM-forming uveal melanoma cells acquire a cancer stem cell-like phenotype that may play a role in the increased therapy resistance of these cells.

### **Biography**

Klara Valyi-Nagy, MD is Research Assistant Professor at the Department of Pathology, University of Illinois at Chicago and Associate Director of the University of Illinois Biorepository. Her primary research interests include three-dimensional cultures in oncology research and tissue banking and extracellular matrix - genome interactions in cancer.

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