Towards Personalized Medicine: Microdevice-Assisted Evaluation of Cancer Stem Cell Dynamics and Treatment Response

Eduardo Imanol Agüero [1,2], **Silvia María Gómez López** [1,3], **Ana Belén Peñaherrera-Pazmiño** [4], **Matías Tellado** [5], **Maximiliano Sebastián Pérez** [6,7,8], **Betiana Lerner** [6,7,8], **Denise Belgorosky** [1,*] and **Ana María Eiján** [1,2,*]

[1]Universidad de Buenos Aires, Facultad de Medicina, Instituto de Oncología Ángel H. Roffo, Área de Investigación, Buenos Aires C1417DTB, Argentina
[2]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ciudad Autónoma de Buenos Aires C1425FQD, Argentina
[3]Agencia Nacional de Promoción de la Investigación, el Desarrollo Tecnológico y la Innovación, Fondo para la investigación Científica y Tecnológica (FONCyT), Ministerio de Innovación, Ciencia y Tecnología (MINCyT), Ciudad Autónoma de Buenos Aires C1425FQD, Argentina
[4]Centro de Investigación Biomédica (CENBIO), Facultad de Ciencias de la Salud Eugenio Espejo, Universidad UTE, Quito 170527, Ecuador
[5]VetOncologia-Clínica Oncológica Veterinaria, Buenos Aires C1408BGD, Argentina
[6]Centro IREN, Universidad Tecnológica Nacional (UTN), Buenos Aires B1706EAH, Argentina
[7]Collaborative Research Institute Intelligent Oncology (CRIION), 79117 Freiburg im Breisgau, Germany
[8]Department of Electrical and Computer Engineering, Florida International University, Miami, FL 33174, USA*Authors to whom correspondence should be addressed.

Abstract

Cancer stem cells are a distinct subpopulation within tumors that possess the ability to self-renew, resist treatment, and drive tumor recurrence. Their identification and characterization are essential for developing more effective and personalized cancer therapies. In this study, we established a microdevice-based platform that enables the growth of three-dimensional cancer spheres from both established cancer cell lines and primary tumor samples. We demonstrated its utility by assessing the effect of chemotherapy on cancer spheres and by analyzing tumors from veterinary patients. Our findings suggest that this platform could be a valuable tool for advancing research in human and veterinary oncology, supporting the development of targeted treatment strategies.

Methodology

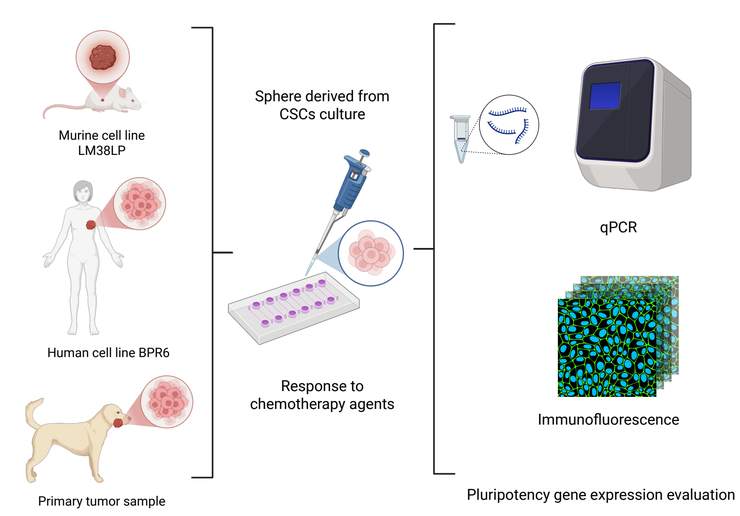

Figure 1. Murine (LM38LP) and human (BPR6) breast cancer cell lines were cultured within MDs to promote sphere formation. CSC enrichment was confirmed through the expression analysis of pluripotency-associated genes) by qPCR and immunofluorescence. Sphere number ,size, and gene expression profiles were quantitatively assessed before (control) and after chemotherapeutic exposure. To extend translational relevance, three primary canine tumor samples were assessed.

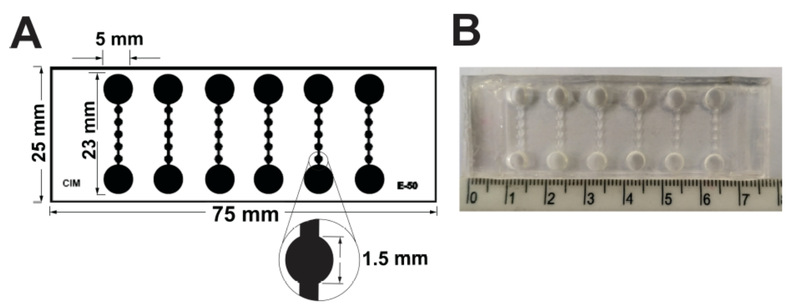

Figure 2. Microfluidic device (MD) comprises 6 independent channels. (B) Photograph of the actual MD.

Results

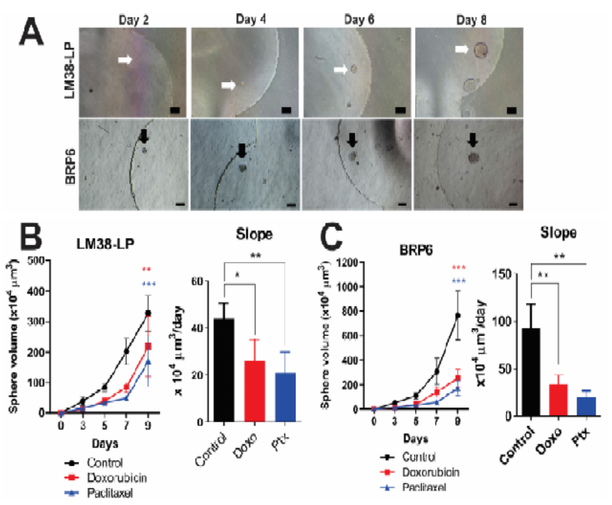

Figure 3. Individual growth of tumor spheres under control and chemotherapeutic treatment conditions in MDs. (A) Images of LM38-LP and BRP6 spheres growing at different time points. Arrows indicate the spheres selected for growth monitoring. Bars represent the mean ± standard deviation from at least 4 experiments. (B,C) Two-way ANOVA and one-way ANOVA for slope analysis, both with Dunnett's multiple comparisons (* $p < 0.05$, ** $p < 0.005$, *** $p < 0.00005$). Scale bar: 100 µm..

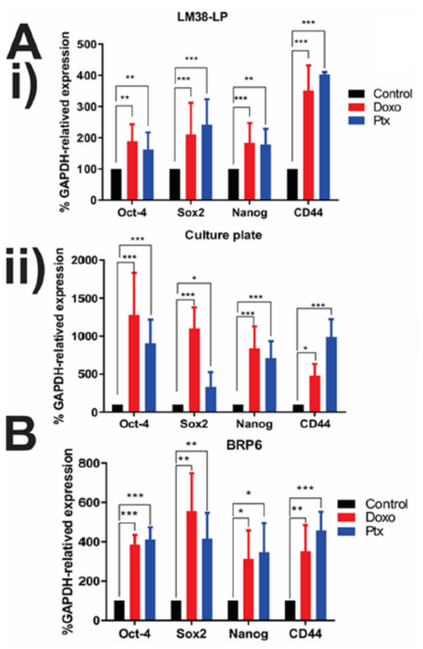

Figure 4. Pluripotency genetic markers in spheres under chemotherapeutic treatment by qPCR and IF. (A)GAPDH-related expression of Oct-4, Sox2, Nanog, and CD44 mRNA in LM38-LP spheres growing in (i) MDs and (ii) culture plate and (B) in BRP6 spheres.

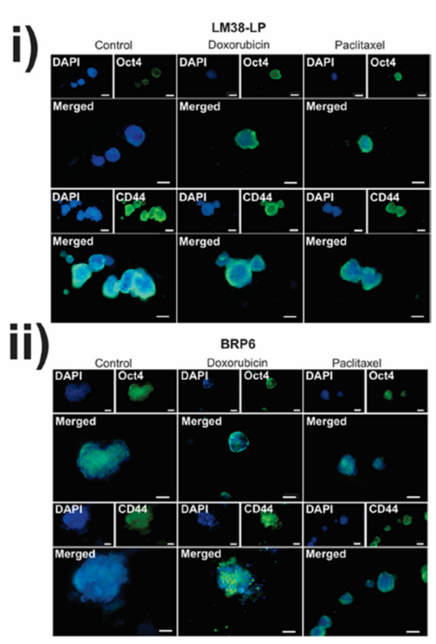

Figure 5. Images of IF Alexa ®488 staining for Oct4 and CD44 in (i) LM38-LP and (ii) BRP6 spheres inside the device. Both techniques were used for control spheres and 7-day treated ones. Scale bar 100 µm

Conclusion

These results highlight the relevance of CSC analysis as a central component in both precision oncology and the study of cancer stem cell biology. Furthermore, our findings demonstrate the versatility of the microdevice platform, which integrates several key features for this type of research, including minimal sample and reagent requirements, and a culture environment well-suited for sphere formation from murine and human tumor cell lines. Notably, we achieved CSC-enriched cultures not only from established models but also from primary murine tumors and canine patient samples, underscoring the potential of this system as a predictive platform for evaluating therapeutic response in both experimental and clinical oncology settings.

Reference

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