



3D POLYMER SCAFFOLDS FOR HIGH THROUGHPUT CELL-BASED ASSAY SYSTEMS

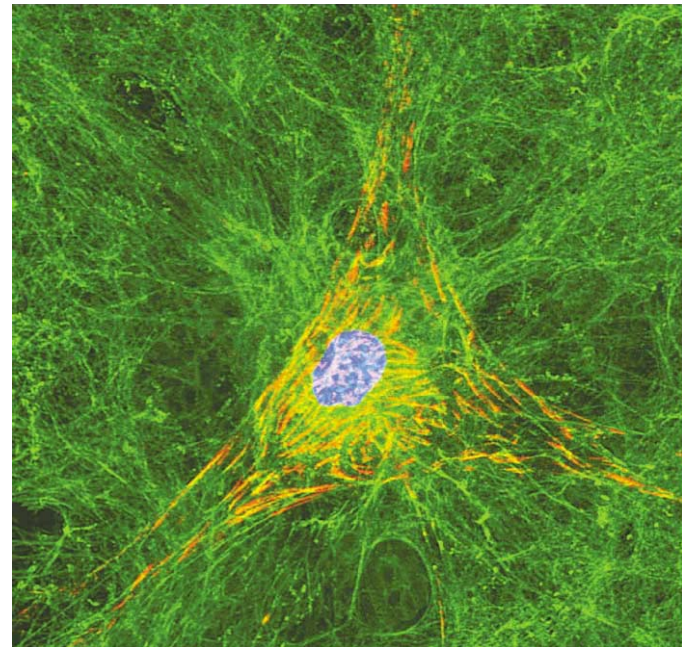
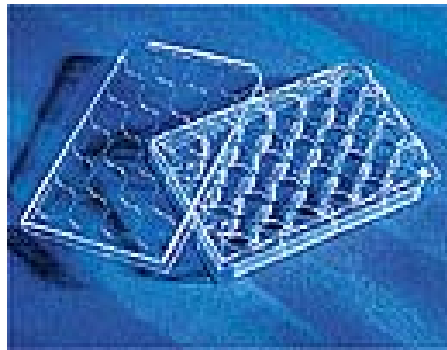
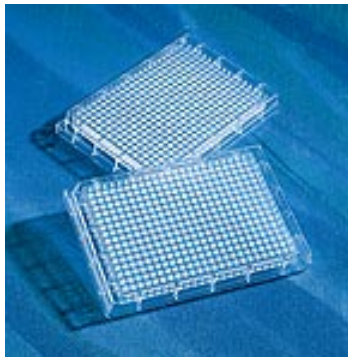
Ke Cheng¹, Yinzhi Lai¹, William S. Kisaalita^{1,2}

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2. Faculty of Engineering
University of Georgia, Athens, GA*

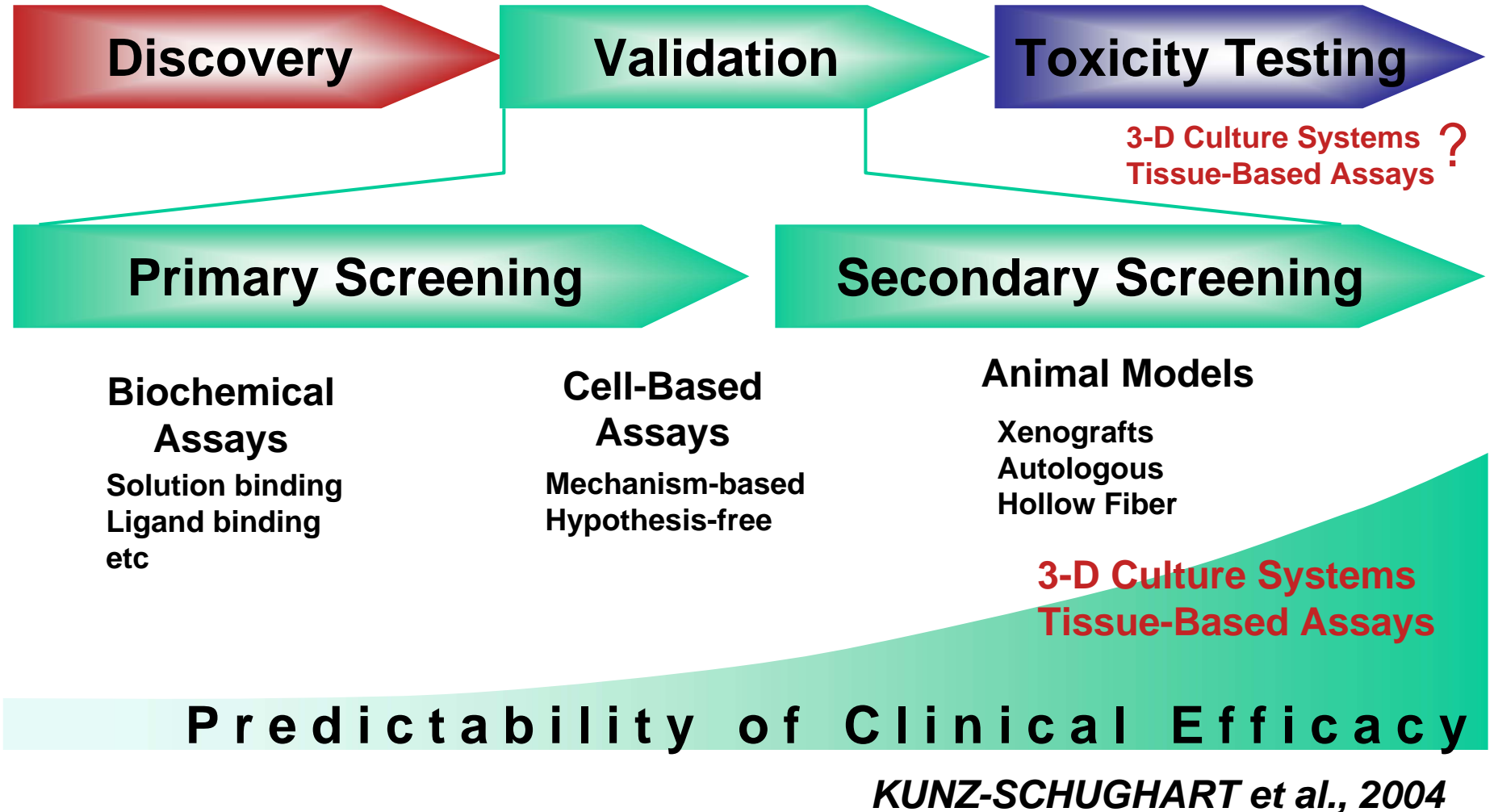
Physiological Relevance of 3-D Cell Culture

“There’s a **big difference** between a flat layer of cells and a complex, three dimensional tissue. But until recently, many biologists have glossed over this fact.”

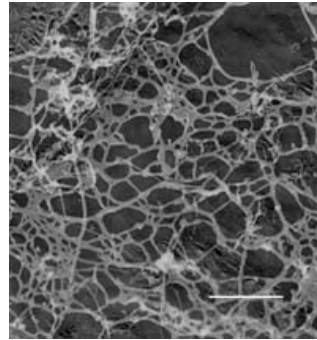
Abbott, A. Nature 424, 870-872, (2003)



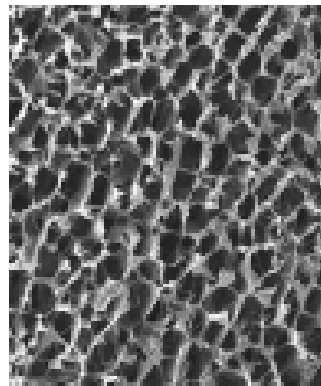
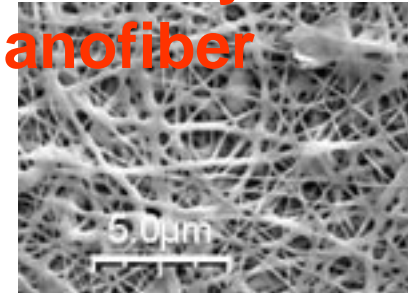
3D Culture for Drug Discovery



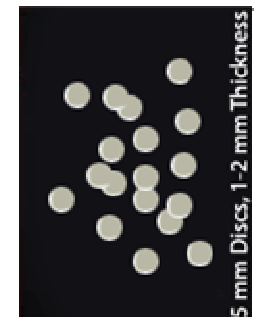
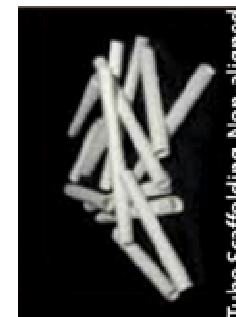
PuraMatrix™



Corning® Ultra-Web™ Synthetic Nanofiber

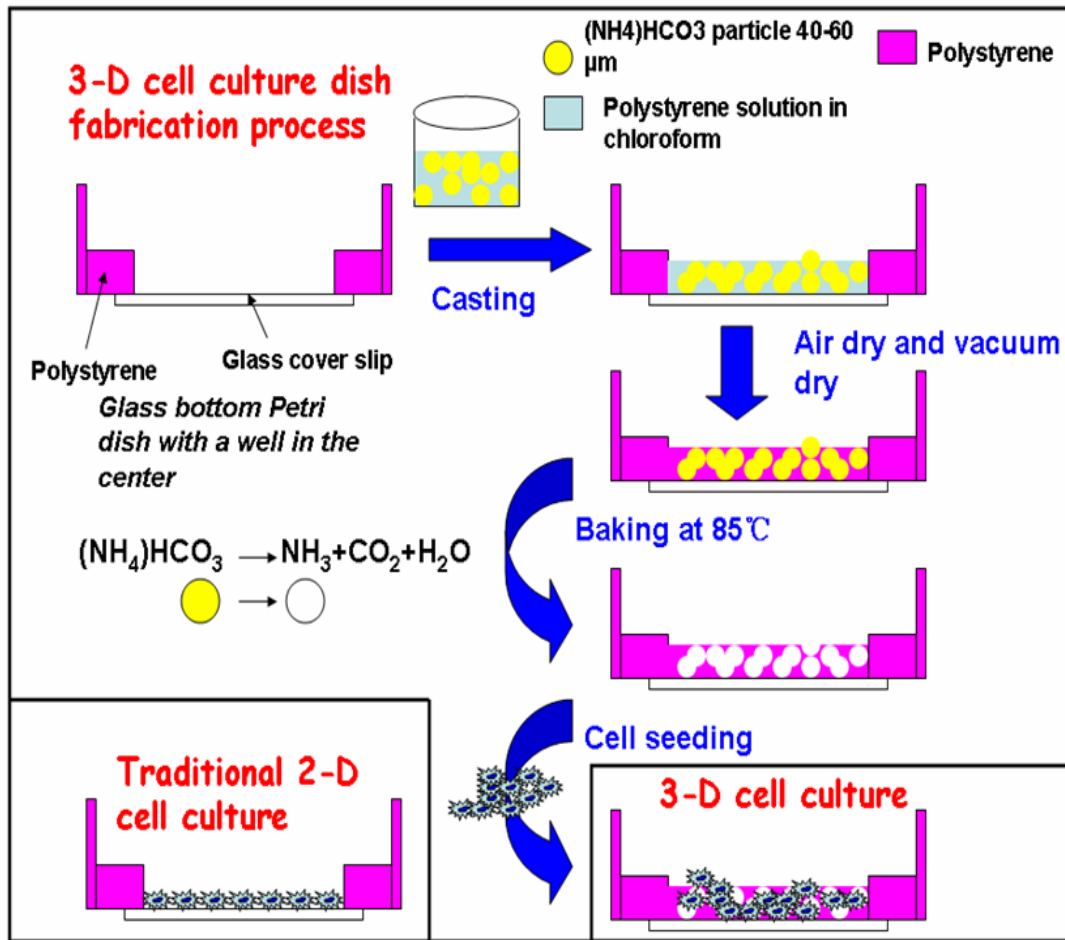
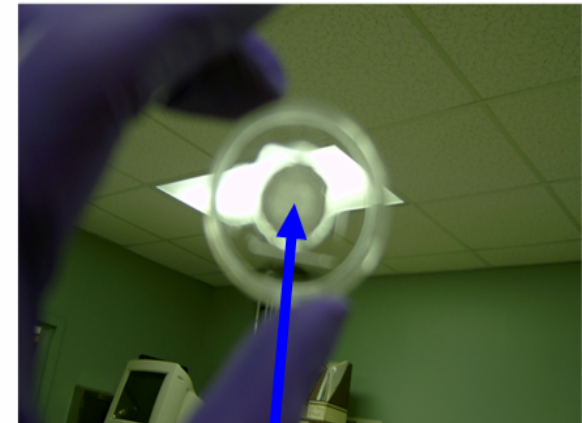
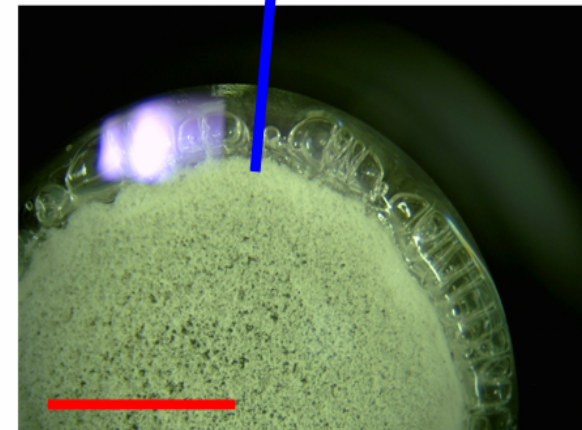


GIBCO® AlgMatrix™ 3D Culture System

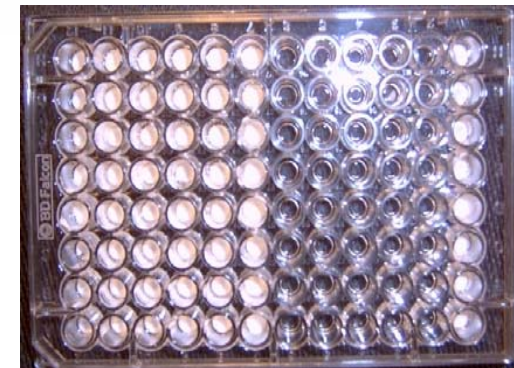
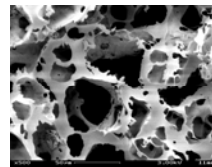


Objective

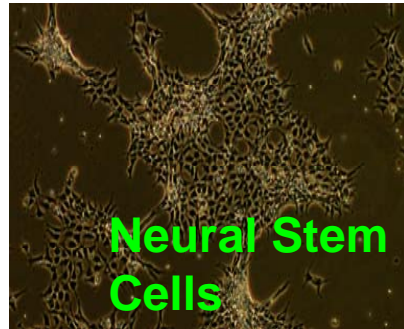
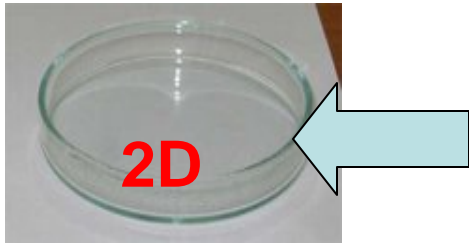
- Create a HTS 3D Cell-based Assay System
- Evaluate the system to see whether cells cultured on it can emulate cells in vivo

a**b****c****Advantages:**

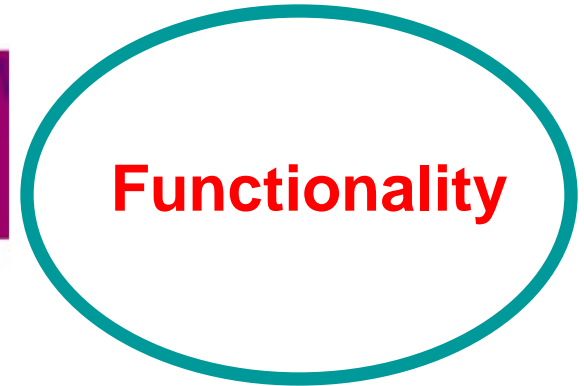
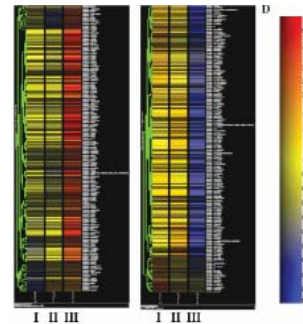
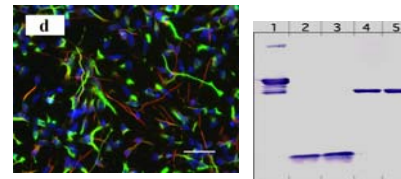
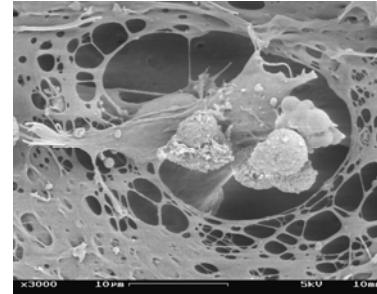
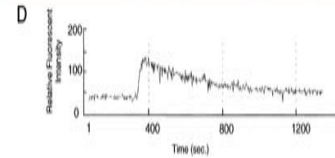
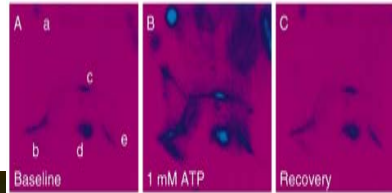
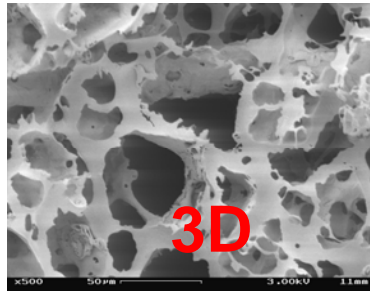
- ✓ Ready-to-use convenience
- ✓ Animal/herbal-free
- ✓ HTS compatibility



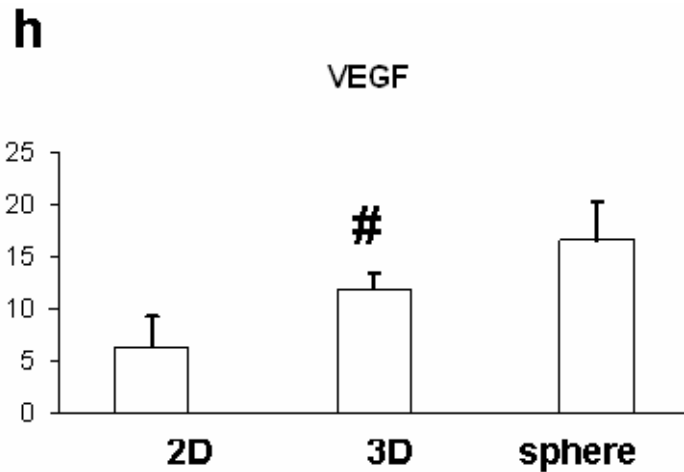
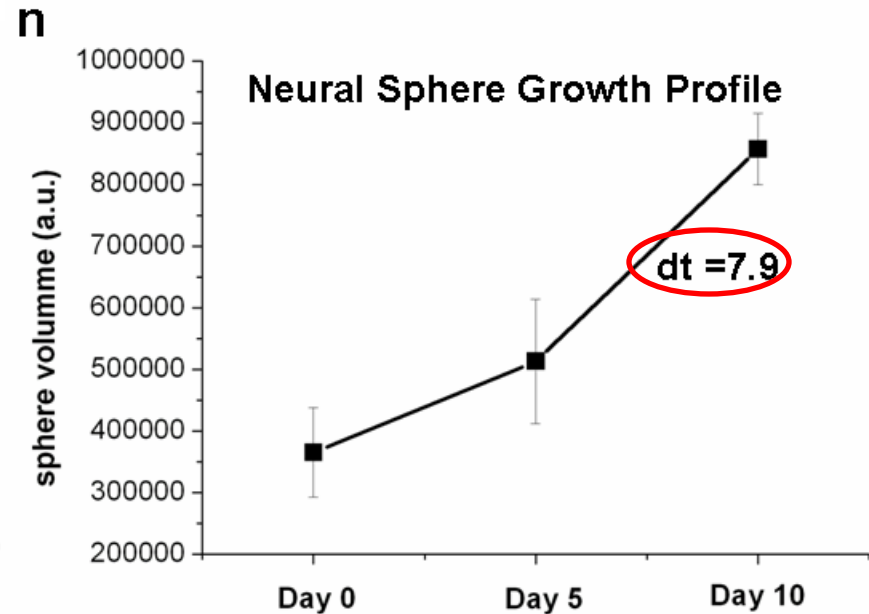
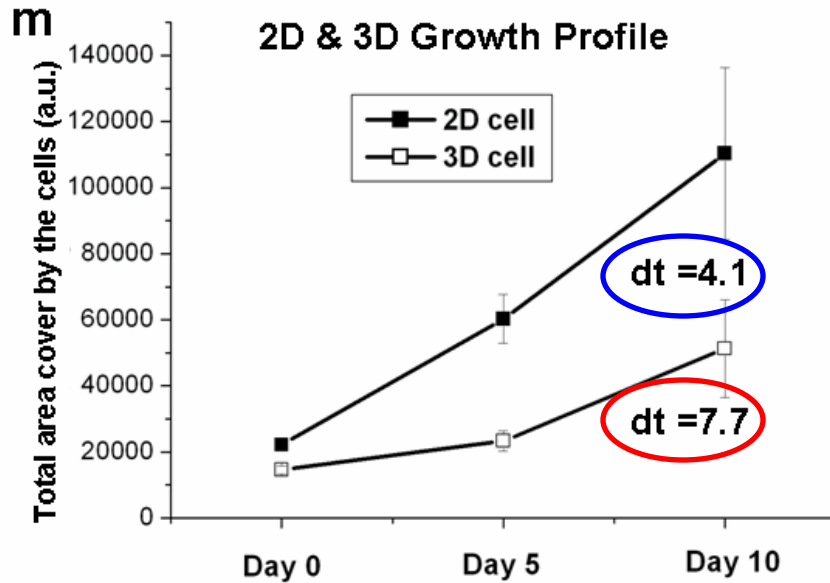
Methods



in vivo
surrogates



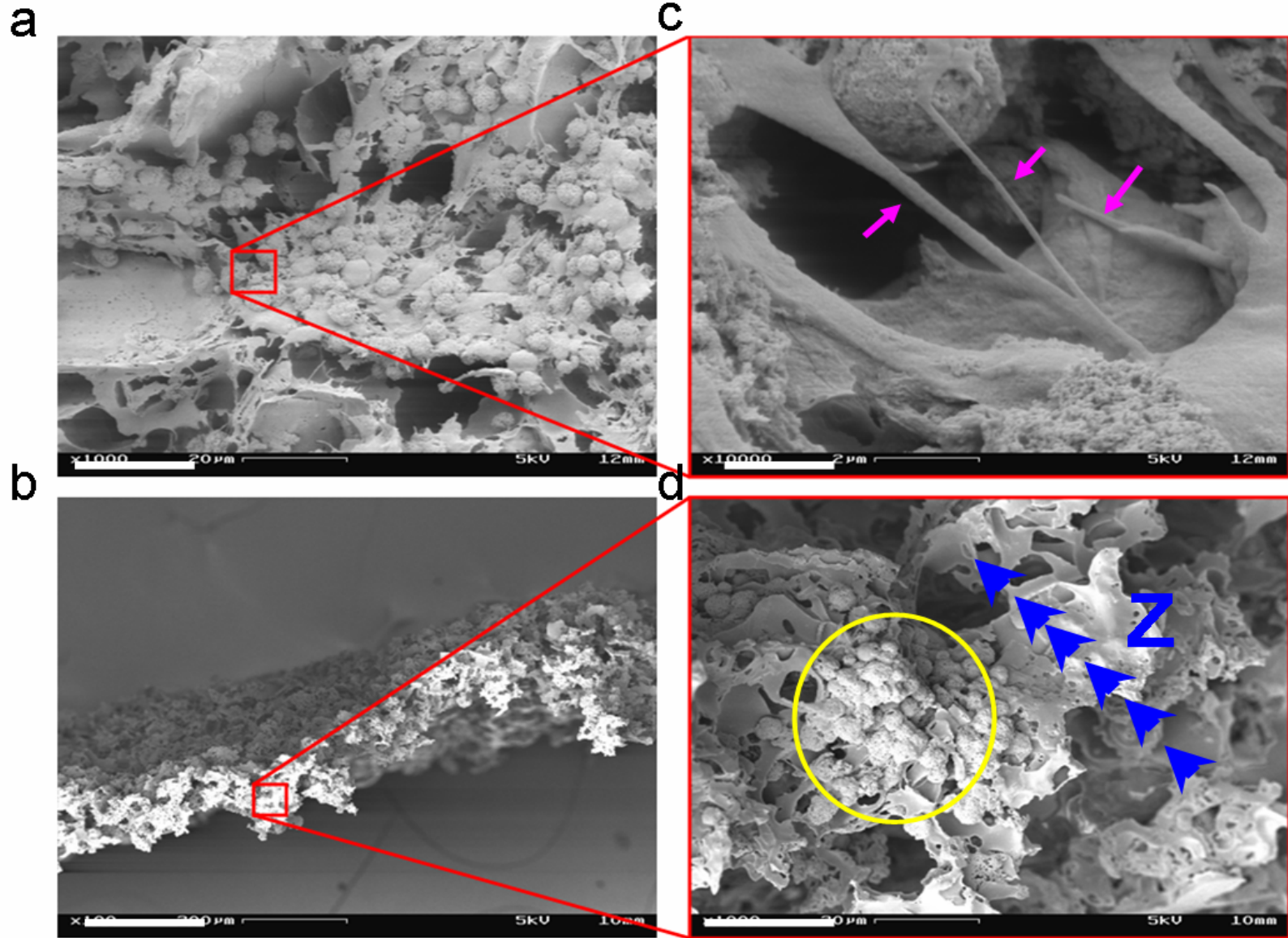
Growth Profile (Proliferation)



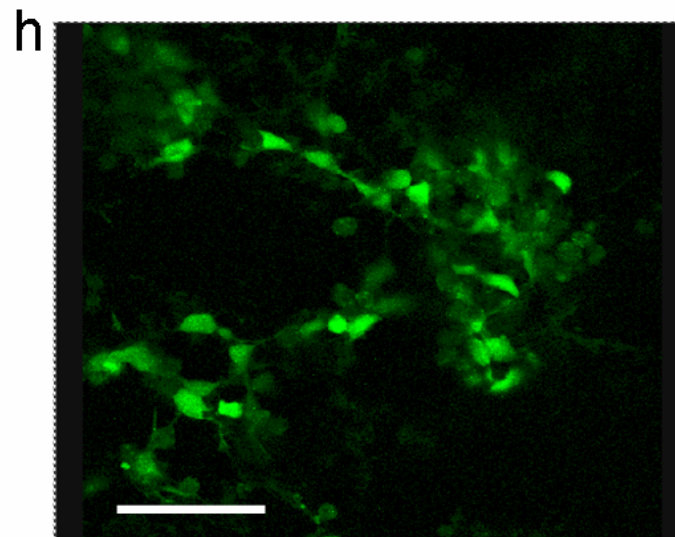
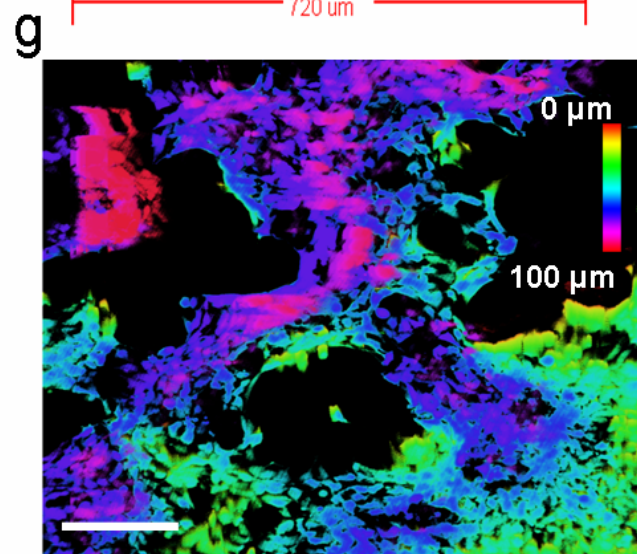
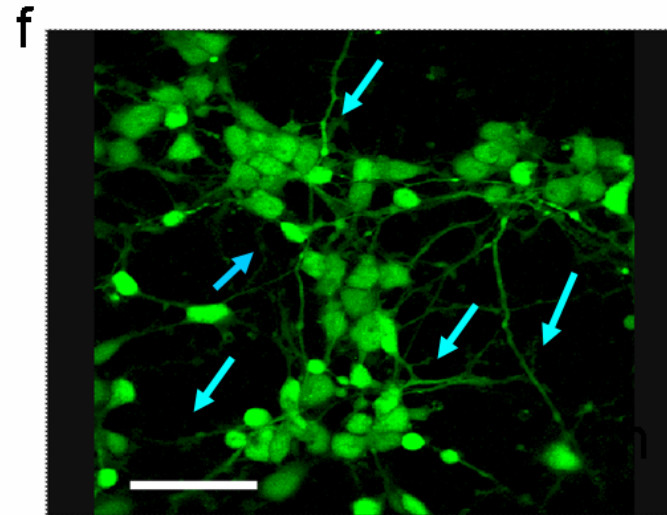
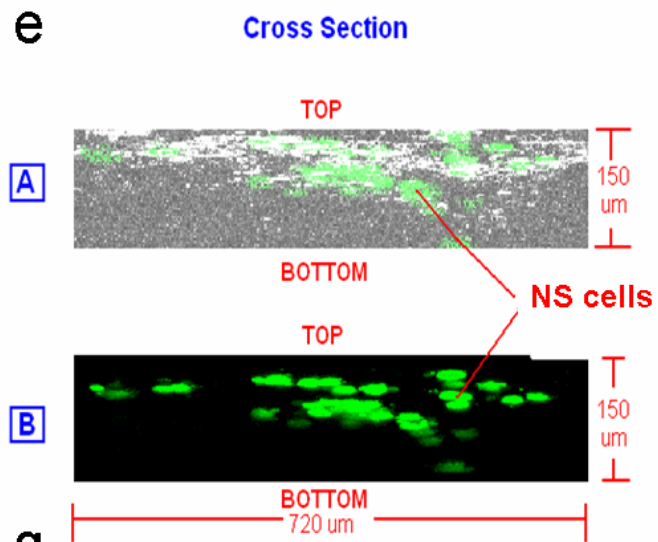
VEGF has effect on proliferation

Meng H et al. Neuroscience Letter. 2006;393(2-3):97-101

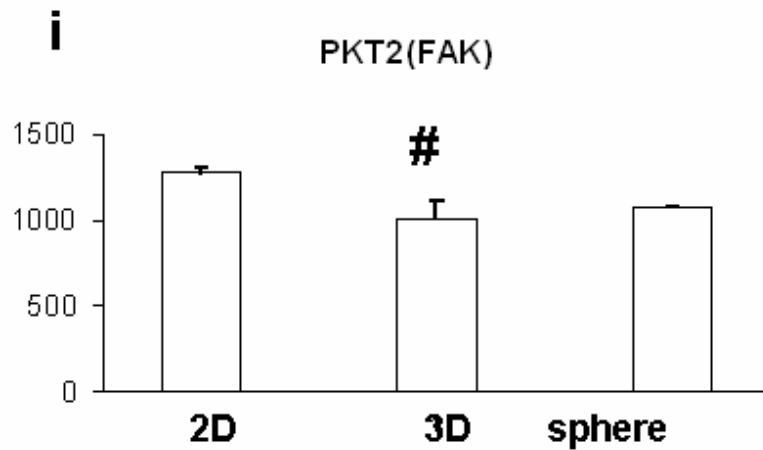
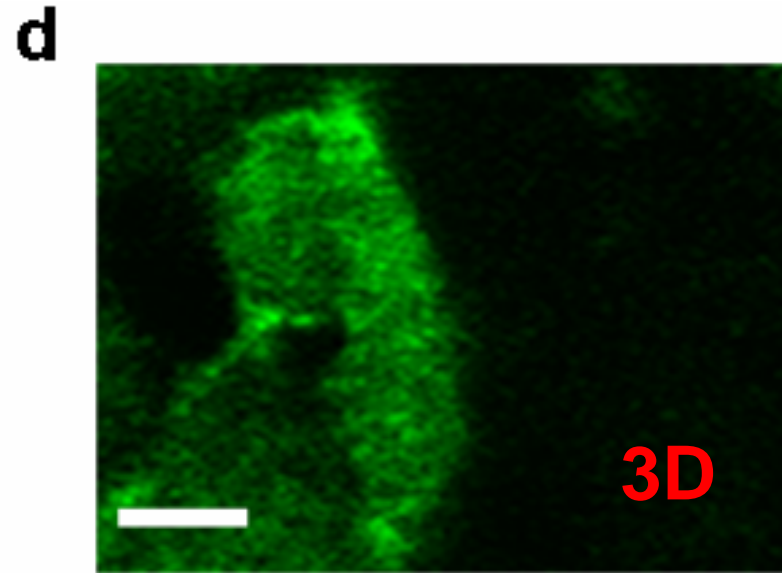
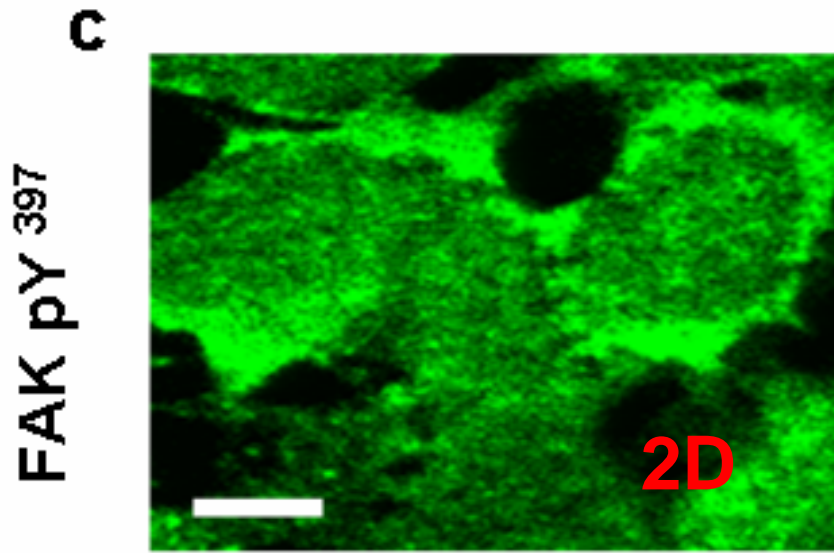
Morphology



Morphology



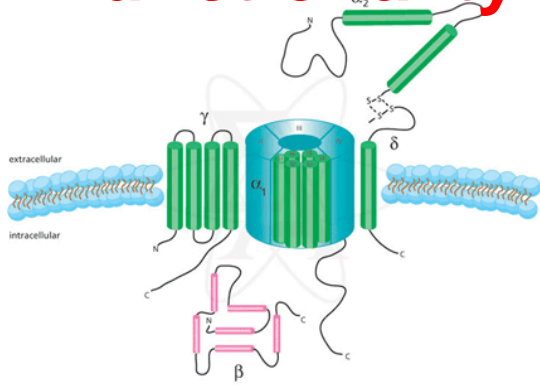
Cell-Matrix Adhesion (FAK pY397)



**FAK loss in “3D
adhesion”!**

***Cukierman E et al. Science
2001;294:1708-383.***

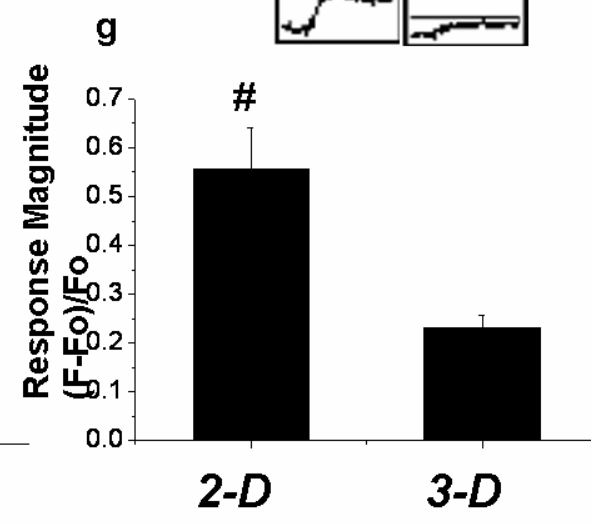
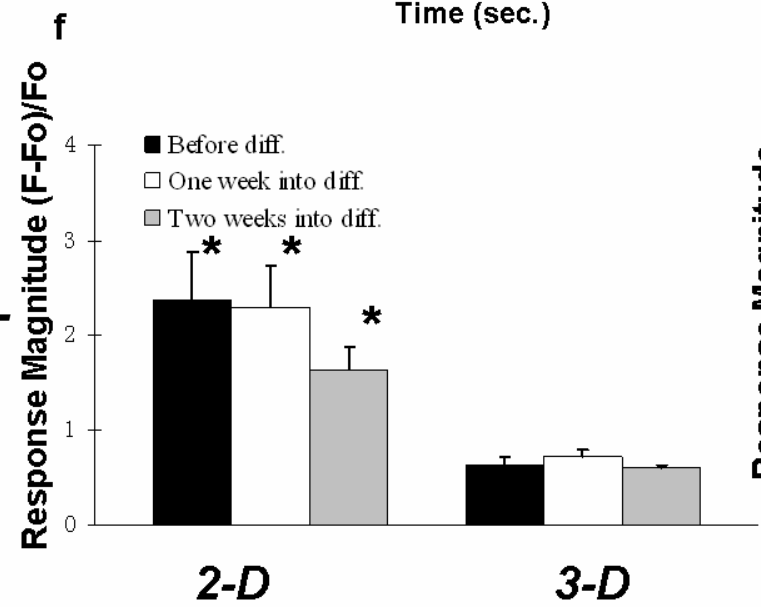
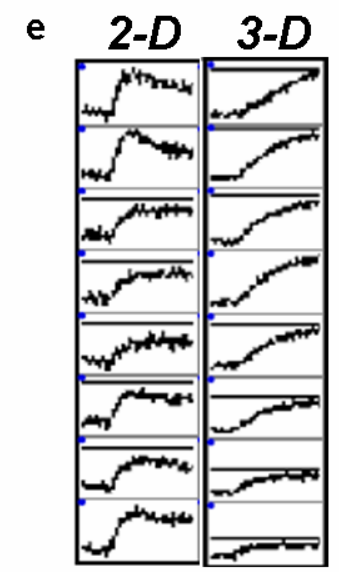
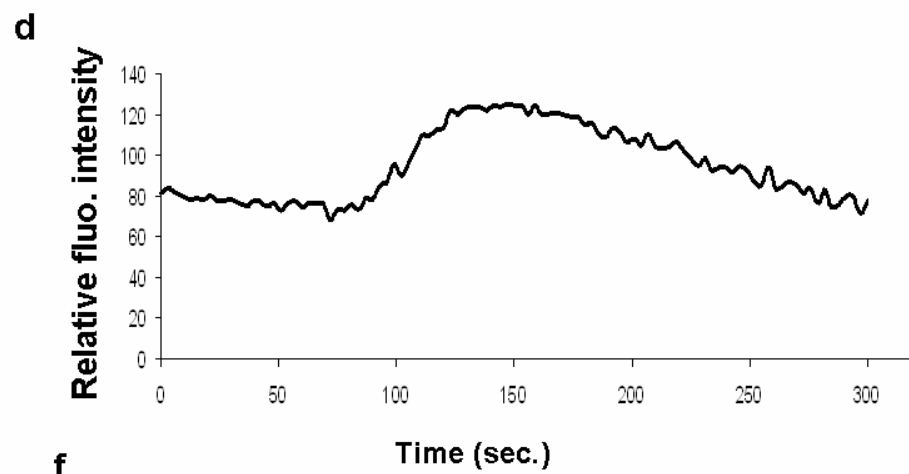
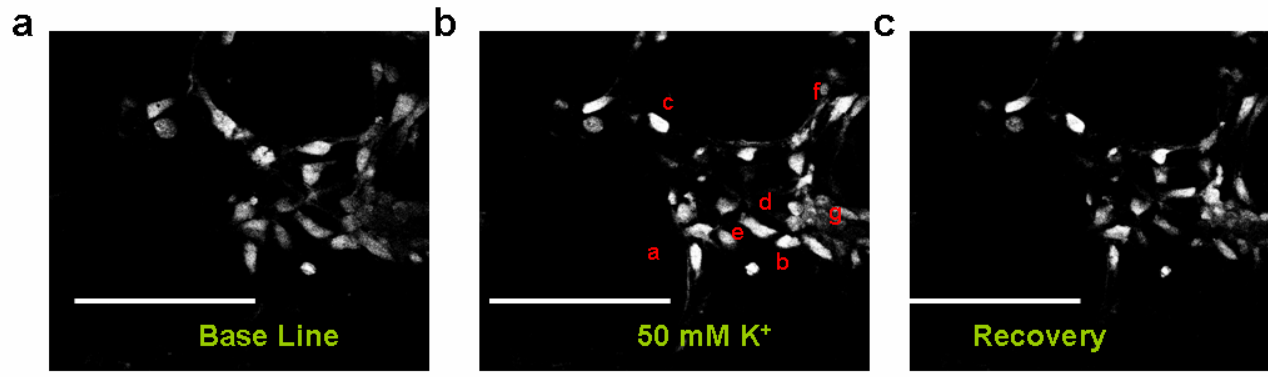
VGCC Functionality



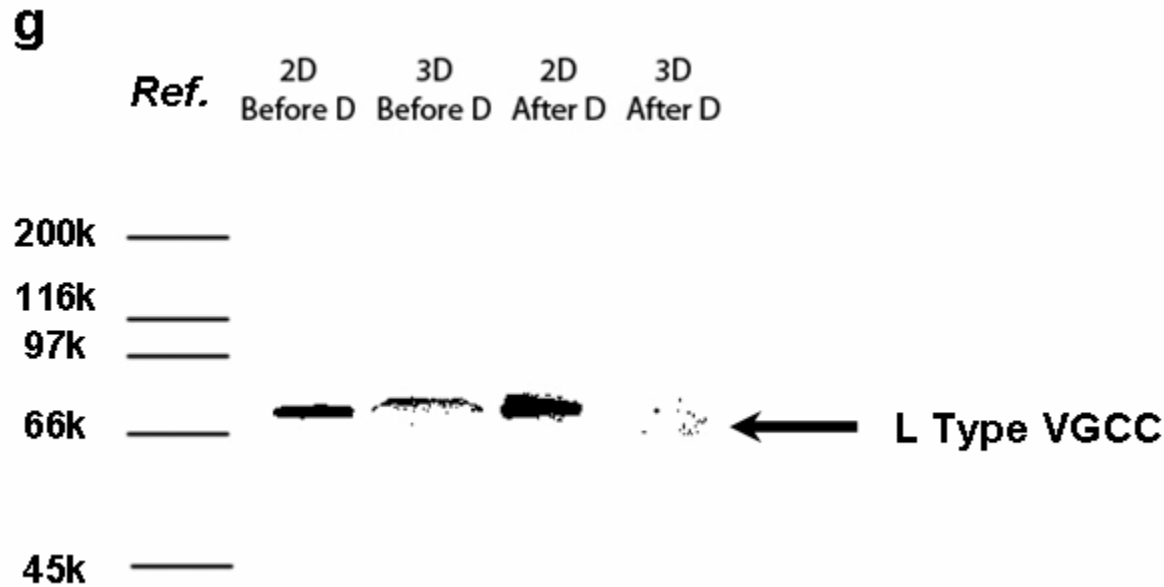
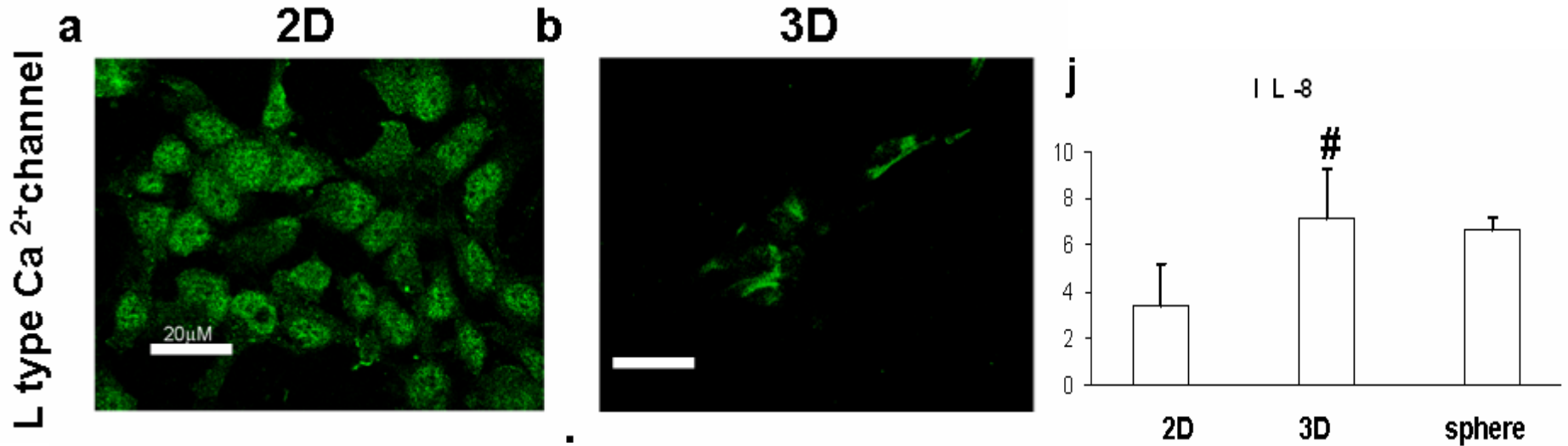
2D Exaggeration!

Wu et al. Biosensors and Bioelectronics 2006;22(5): 685-693.

Cukierman et al. Science 2001;294:1708-383.



Calcium Channel Expression



**IL-8 → [Ca²⁺]
current!**

*Puma et al. Journal of
Neurochemistry.
2001;78(5): 960-71*

Summary

	2D Cells	3D Cells	In vivo surrogates
Proliferation	+	-	-
FAK gene expression	+	-	-
IL-8 gene expression	-	+	+
VEGF gene expression	-	+	+
L-type Calcium Channel protein	+	-	n/a
VGCC activity	+	-	n/a

“+” denotes that the gene is up-regulated, the protein is up-expressed or the cellular activity is higher in comparison to the groups marked with “-”.

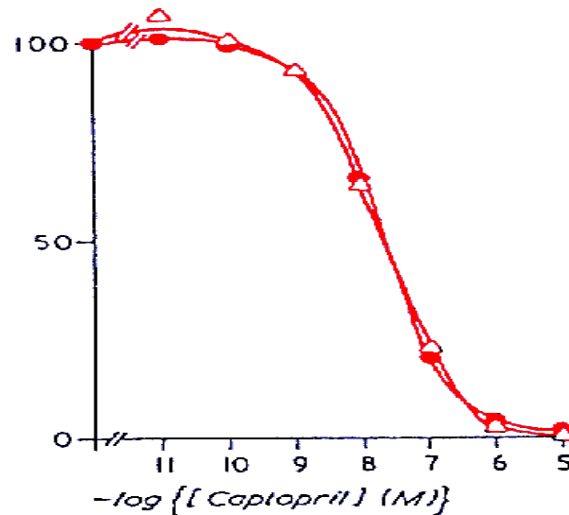
“-” denotes that the gene is down-regulated, the protein is down-expressed or the cellular activity is lower in comparison to the groups marked with “+”.

Conclusion

- This 3-D cell cultured systems can support long term cell growth and differentiation
- Cells growing on our 3-D culture systems **more closely mimic in vivo** than 2-D cultured cells, with respect to cell morphology, proliferation, adhesion, and VGCC functionality.
- This 3-D cell-based assay systems can be incorporated into any current HTS systems in use today

Future work

- Compare IC50s of cells on 2-D, 3-D and in vivo by exposing them to drugs



- Create novel scaffold types

Acknowledgement



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WHERE DISCOVERIES BEGIN

Dr. Kisaalita

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Dr. John Shields

Dr. Steve Stice

Dr. Z.Z. Wu

Ms. Lina Wang

Mr. Rahul Singh



Thanks!