POTENTIAL ENERGY

Leaving the Scientific Comfort Zone to Address Complex Challenges

Ayala Lampel[1,*]

Dr. Ayala Lampel is a postdoctoral research associate in Prof. Rein Ulijn's research group in the Nanoscience Initiative at the CUNY Advanced Science Research Center and an awardee of an Israeli Council for Higher Education Postdoctoral Fellowship. Her work focuses on designing functional supramolecular materials for biological systems. Before this, Ayala received her PhD in biotechnology at Tel Aviv University, where she worked with Prof. Ehud Gazit on viral capsid assembly and antiviral design tools, and her BSc in neuroscience (BSc Program in Neuroscience for Outstanding Students, Tel Aviv University). During her PhD, Ayala volunteered in the Israeli association "Bashaar" to introduce scientific higher education to underprivileged high school students.

In this issue of *Chem*, our study, "Tunable Supramolecular Hydrogels for Selection of Lineage-Guiding Metabolites in Stem Cell Cultures,"[1] shows that chemistry can help answer a fundamental biological question—how do

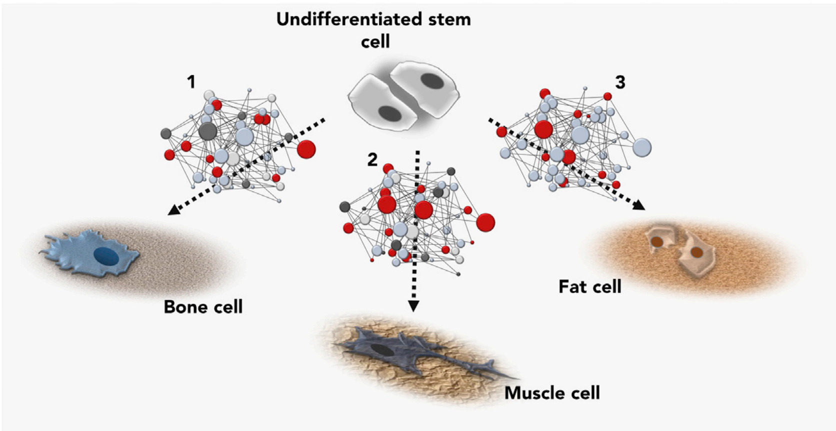

Figure 1. Using Different Biomaterial Designs to Direct Stem Cell Fate, which Allows Profiling of Divergent Cell Kinetics—1, 2, and 3—that Give Rise to a Number of Specialized Cell Types

us to discuss the required properties and to design material systems by using chemistry. Design suddenly moves a wholesome biologist into the field of surface patterning, adhesion chemistries, and much more. Working at the cell-material interface means straddling these worlds and finding out how they come together. This in itself fosters being multidisciplinary—you do not simply fall through the rabbit hole, so to speak; instead, you spend a lot of time wandering through and tending to it.

So then, for all its peculiarities and mental adjustments, how has the criss-crossing of scientific disciplines (as well as academia and industry) enabled me thus far? In a nutshell, it has offered a broader perspective on capabilities and opportunities, has helped me develop a better sense of measuring and taking risks, and most importantly, has fostered creativity. In other words, a chemist's biomaterial is not a clinician's biomaterial or a biologist's biomaterial, and more often than not, the answer is one that traverses all boundaries. How many "corridors" you wander, however, is something that is very much up to the individual and the choices he or she makes. An approach of getting around this is through identifying the potential application(s) of your research or design. Application-driven research connotes a common goal. Approaching it through fostering differing disciplines means that the goal can be reached in any number of ways, also highlighting the importance of collaborative projects. This is definitely a powerful way of bridging disciplines, and I would always encourage collaborations that make you reach beyond your comfort zone.

1. Dalby, M.J., Andar, A., Nag, A., Affrossman, S., Tare, R., McFarlane, S., and Oreffo, R.O.C. (2008). J. R. Soc. Interface *5*, 1055–1065.

2. Discher, D.E., Janmey, P., and Wang, Y.L. (2005). Science *310*, 1139–1143.

3. Engler, A.J., Sen, S., Sweeney, H.L., and Discher, D.E. (2006). Cell *126*, 677–689.

4. McMurray, R.J., Gadegaard, N., Tsimbouri, P.M., Burgess, K.V., McNamara, L.E., Tare, R., Murawski, K., Kingham, E., Oreffo, R.O.C., and Dalby, M.J. (2011). Nat. Mater. *10*, 637–644.

5. Jayawarna, V., Richardson, S.M., Hirst, A.R., Hodson, N.W., Saiani, A., Gough, J.E., and Ulijn, R.V. (2009). Acta Biomater. *5*, 934–943.

6. Ulijn, R.V., Bibi, N., Jayawarna, V., Thornton, P.D., Todd, S.J., Mart, R.J., Smith, A.M., and Gough, J.E. (2007). Mater. Today *10*, 40–48.

[1]School of Geographical & Earth Sciences, College of Science & Engineering, University of Glasgow, Gregory Building, Glasgow G12 8QQ, UK

*Correspondence:
enateri.alakpa@glasgow.ac.uk

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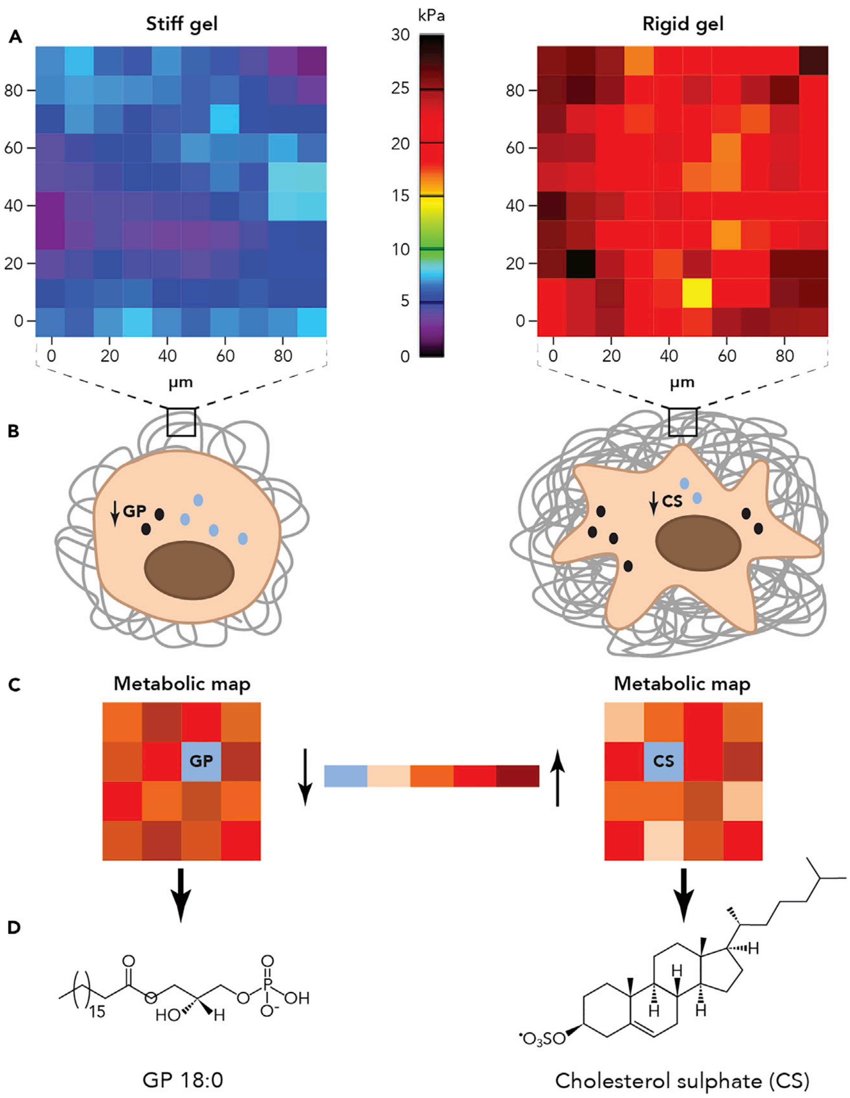

Figure 1. Supramolecular Hydrogels for Metabolomics Analysis of Differentiating Stem Cells
Tuning the hydrogels' stiffness (A, AFM stiffness maps) induced stem cell differentiation into specific phenotypes (B), which further allowed whole-metabolome analysis (C), leading to the identification of key metabolites involved in the differentiation process (D).

stem cell metabolomes respond to physical forces in their environment? Specifically, we designed peptide-based supramolecular biomaterials[2,3] for metabolomics analysis of stem cell differentiation into different lineages. Because the hydrogels are mechanically tunable (Figure 1A), thus triggering differentiation[4] (Figure 1B), and exhibit a much simpler chemical composition than previously used cell-culture matrices, they enable this complex metabolomics analysis (Figure 1C). Using these supramolecular biomaterials, we identified metabolites (simple lipids; see Figure 1D) that are involved in differentiation into a specific cell phenotype and can serve as drug candidates in the future.

Involving supramolecular-materials chemistry, analytical chemistry, and cell biology as well as researchers from 17 different backgrounds, this project was complex. Its success required integrating various approaches and tools by gathering a combination of supramolecular-materials chemists (Prof. Rein Ulijn's group), cell engineers, and metabolomics experts (Prof. Matthew Dalby's group).

Addressing complex scientific challenges such as the one posed here requires vast knowledge and a wide range of expertise, and therefore the real question is, can we really master everything? Probably not, and thus, recognizing that we should engage experts from other fields of science to collaborate with and learn from can be critical. The project started through close collaboration between Dr. Enateri Alakpa and Dr. Vineetha Jayawarna from the Dalby and Ulijn groups, respectively, but as new data gave rise to additional questions, further experts had to be consulted. For example, one of the challenges that I was personally faced with in this study was to characterize the mechanical properties of the designed hydrogels at the micron scale. We realized that for a rigorous analysis, we needed the help of experts in atomic force microscopy (AFM) mechanical measurements. Therefore, we referred to the Molecular Cytology Core Facility at the Memorial Sloan Kettering Cancer Center, which assisted me in performing mechanical analysis of the hydrogels.

My own experience with interdisciplinary science started at the beginning of my PhD in Prof. Ehud Gazit's research group (Tel Aviv University), when I chose to focus on the viral assembly process, which I found particularly intriguing. Although the Gazit lab studies various aspects of molecular self-assembly, this specific area was completely new to us at the time. As a non-virologist with a BSc in neuroscience, I experienced many challenges in exploring this new field. To overcome these challenges, we worked in close collaboration with HIV experts (Prof. Eran Bacharach's research group, Tel Aviv University), from whom I learned various new methods. We combined these virology techniques with biochemical and biophysical tools to gain new insights into HIV self-assembly and develop new therapeutic tools.[5]

I experienced firsthand how the molecular viewpoint is key to any basic understanding and manipulation of the viral self-assembly process, and I became more attuned to this point of view. This led me to choose to do my postdoctoral training in Prof. Rein Ulijn's lab, which focuses on molecular-level understanding and design of supramolecular materials and molecular-level aspects of their function. During the past year, I have already greatly expanded my knowledge of and expertise in characterization tools for supramolecular chemistry, and I intend to further implement them to influence and interrogate biological systems.

The Ulijn lab is part of CUNY's new Advanced Science Research Center, which was conceptually and functionally designed to foster bridging across different disciplines. The center is organized around five thematic initiatives on different floors: nanoscience, photonics, structural biology, neuroscience, and environmental science. The unique architecture and frequent meetings of all the center's members trigger cross-talk between us, scientists from different disciplines, and provide a platform for facilitating interdisciplinary and cross-disciplinary communication.

Accomplishing interdisciplinary or cross-disciplinary science remains challenging, particularly regarding how far one should step outside one's scientific comfort zone. In our project, each of us adapted our own scientific agenda along the way. Whereas some of us view every aspect of science at the molecular level, others perceive science at the cellular, whole-system, or even whole-organism level. Can we ever bridge the gap between these extremely different perspectives? As someone who navigates between these viewpoints, both in my present work and in my anticipated academic career, I wish to find a way to overcome this challenge and to be able to observe and think about biomedical science questions at both the molecular and cellular levels by using a supramolecular-systems approach.[6]

1. Alakpa, E.V., Jayawarna, V., Lampel, A., Burgess, K.V., West, C.C., Bakker, S.C.J., Roy, S., Javid, N., Fleming, S., Lamprou, D.A., et al. (2016). Chem *1*, this issue, 298–319.

2. Zhang, S. (2003). Nat. Biotechnol. *21*, 1171–1178.

3. Webber, M.J., Appel, E.A., Meijer, E.W., and Langer, R. (2016). Nat. Mater. *15*, 13–26.

4. Engler, A.J., Sen, S., Sweeney, H.L., and Discher, D.E. (2006). Cell *126*, 677–689.

5. Lampel, A., Bram, Y., Ezer, A., Shaltiel-Kario, R., Saad, J.S., Bacharach, E., and Gazit, E. (2015). ACS Chem. Biol. *10*, 1785–1790.

6. Grzybowski, B.A., and Huck, W.T. (2016). Nat. Nanotechnol. *11*, 585–592.

[1]Nanoscience Initiative, CUNY Advanced Science Research Center, New York, NY 10031, USA

*Correspondence: lampelayala@gmail.com

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