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Appendices

About the author
List of publications
Acknowledgements

About the author

Darinka Klumpers was born on May 9th, 1985 in Leiden, The Netherlands. After receiving her high school diploma from the Stedelijk Gymnasium Leiden in 2003, she started her bachelors studies in Medical Natural Sciences at the VU University in Amsterdam. This young degree program aims to bridge the disciplines of biology, medicine, physics, chemistry, and engineering and stimulates interdisciplinary collaboration, communication and research. During her bachelors studies she performed two scientific research internships. At the department of Physics and Medical Technology at the VU University Medical Center she investigated new model systems to study the role of substrate stiffness on stem cell behavior under the supervision of Dr. R.G.M. Breuls. Second, at the department of Medical Oncology at the Cancer Center Amsterdam, she optimized cell viability assays for usage in genome wide high throughput screenings under the supervision of Dr. V.W. van Beusechem.



After completion of her bachelors degree in 2006, she continued to study at the VU University engaging in a research-focused masters program in Medical Physics. She returned to the department of Physics and Medical Technology at the VU University Medical Center to continue to work with Dr. R.G.M. Breuls, investigating the interdependent effects of substrate stiffness and matrix composition on fibroblast behavior. Eager to explore science at the international level, she traveled to Boston for an eight-month research internship at the Harvard School of Public Health, supported by a HSP Talent Program fellowship. Under the supervision of Dr. R. Krishnan in the laboratory of Prof. dr. J.J. Fredberg, she investigated the role of substrate stiffness and cellular force generation on endothelial monolayer integrity.

Captured by the ambition and excitement of the scientific community in Boston, she decided to engage in a PhD opportunity that would allow her to stay in Boston after obtaining her masters degree in 2009. As such, she performed her PhD research in the laboratory for Cell and Tissue Engineering at the School of Engineering and Applied Sciences at Harvard University. She was jointly supervised by Prof. dr. ir. T.H. Smit at the VU University Medical Center in Amsterdam and Prof. dr. D.J. Mooney at Harvard University in Boston.

List of publications

1. C. Branco da Cunha, **D.D. Klumpers**, W.A. Li, S.T. Koshy, J.C. Weaver, O. Chaudhuri, P.L. Granja, D.J. Mooney. *Influence of the stiffness of three-dimensional alginate/collagen-I interpenetrating networks on fibroblast biology*. *Biomaterials*. 2014 Oct;35(32):8927-36
2. **D.D. Klumpers**, A.S. Mao, T.H. Smit, D.J. Mooney. *Linear patterning of mesenchymal condensations is modulated by geometric constraints*. *J Royal Society Interface*. 2014 Apr 9;11(95):20140215
3. **D.D. Klumpers**, X. Zhao, D.J. Mooney, T.H. Smit. *Cell mediated contraction in 3D cell-matrix constructs leads to spatially regulated osteogenic differentiation*. *Integrative Biology (Camb)*. 2013 Sep;5(9):1174-83
4. R. Krishnan*, **D.D. Klumpers***, C.Y. Park, K. Rajendran, X. Trepas, J. van Bezu, V.W. van Hinsbergh, C.V. Carman, J.D. Brain, J.J. Fredberg, J.P. Butler, G.P. van Nieuw Amerongen. *Substrate stiffening promotes endothelial monolayer disruption through enhanced physical forces*. *Am J Physiol Cell Physiol*. 2011 Jan;300(1):C146-54.
5. R.G.M. Breuls, **D.D. Klumpers**, V. Everts, T.H. Smit. *Collagen type V modulates fibroblast behavior dependent on substrate stiffness*. *Biochem Biophys Res Commun*. 2009 Mar 6;380(2):425-9.
6. O. Chaudhuri*, L. Gu*, **D.D. Klumpers**, M. Darnell, S.A. Bencherif, J.C. Weaver, N. Huebsch, D.J. Mooney. *Hydrogels with tunable stress relaxation properties to regulate stem cell fate and activity*. In revision at Nature Materials
7. O. Chaudhuri*, L. Gu*, M. Darnell, **D.D. Klumpers**, S.A. Bencherif, J.C. Weaver, N. Huebsch, D.J. Mooney. *Substrate stress relaxation regulates cell spreading*. In revision at Nature Communications
8. **D.D. Klumpers**, D.J. Mooney, T.H. Smit. *From skeletal development to tissue engineering: lessons from the micromass assay*. Submitted for publication
9. **D.D. Klumpers**, T.H. Smit, D.J. Mooney. *The effect of growth-mimicking continuous strain on the early stages of skeletal development in micromass culture*. Submitted for publication
10. C. Branco da Cunha, **D.D. Klumpers**, J.C. Weaver, O. Chaudhuri, F. Carneiro, P.L. Granja, D.J. Mooney. *Matrix dimensionality and stiffness instruct CD44 alternative splicing in gastric cancer cells*. Submitted for publication

*Authors contributed equally to this work

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First of all, I would like to thank the committee for taking interest in my work by critically reading my manuscript. I appreciate your effort and consideration.

I have been spoiled with two great advisors, one on each side of the ocean, Theo in Amsterdam and Dave in Boston. Their styles of advising complemented each other, and they always made sure I wouldn't get stuck in the middle. And it worked out great.

Theo, the way you look at biological processes from a mechanical perspective fascinated me from the moment I started working in your group during my masters. Your bold hypotheses and limitless scientific curiosity engaged me. Together, we made this unconventional PhD happen, for which I cannot thank you enough. You were open-minded, didn't back off when the Dutch bureaucracy was giving us a hard time, or when money was hard to find. Over the years, most of our meetings took place on Skype, but the distance and the time-difference never deterred you from being a great and devoted advisor. Thank you, for making this happen, for teaching me great science, and for being there for me every step of the way.

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I had the pleasure to collaborate with a group of great scientists on a range of interesting projects. On the projects described in this thesis, Xuanhe Zhao and Angelo Mao have been invaluable. Xuanhe became enthusiastic about my results before I did, and then helped me by creating a computational model that complemented my experiments. Angelo introduced me to the art of micropatterning and was key from fabricating the devices at the start of the project to performing the image analysis at the end.

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we were able to do so in the end! Ovi and Luo, I will never forget those experiments with 200 million cells, that was real teamwork! So much more fun than doing it alone.

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Cristiana, we shared so much more than our European heritage and our visiting-student status. So many coffees, chats, drinks, dinners. We took care of each other's experiments when necessary, and helped each other through frustrating times.

And the girls! Catia, Christine, Gail, Cristiana, and Erin, while all in the midst of our PhDs, we organized VDC and movie nights. A great way to blow off some steam, spend time together and enjoy sushi, Thai, Indian, etc. And of course there were the girl-nights out and our memorable trip to Montreal! Great times, girls!

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