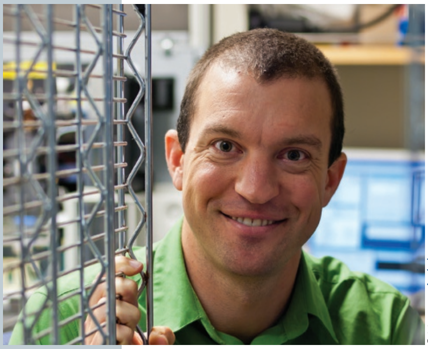
THE AUTHOR FILE

Zev Gartner

Creative chemical techniques to better understand tissue self-organization.

Tissue is togetherness. It's three-dimensional, self-organized, dynamic, biological material in which cells are moving, dividing, dying, and exchanging chemical, electrical and mechanical signals with one another, all of which keeps tissue in balance. Cellular identity in tissue is a function of which cells talk to one another and who their neighbors are, says chemist Zev Gartner of the University of California at San Francisco (UCSF).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A desire to reconstitute that dynamic outside of the context of normal tissue development led Gartner to develop DNA-programmed assembly of cells (DPAC), with which it is possible to build complex tissues with pre-designed, heterogeneous and tailored spatial arrangements by using DNA as a way to stick cells in desired spots. Such lab-grown tissues can help researchers discover the key directors of self-organization and give them a better understanding of how they might help tissues self-organize, Gartner says.

DPAC is versatile. It lets researchers put a cell at any desired position in the tissue-to-be, says Gartner. An experimenter can tease out the features of human tissues to model a disease or to show a particular kind of collective cell behavior. DPAC can help labs test physical or mathematical models of cell-group behavior or explore whether a specific cell with a genetically altered cell-adhesion molecule shows different behavior when embedded in tissue and surrounded by other cells.

Some labs grow tissue in miniaturized organs called organoids, via a process that starts with stem cells. But, says Gartner, it is hard to alter cells in organoids as precisely as with DPAC.

The first stage in DPAC resembles the early stages of city planning, says Gartner. A blueprint is made, and zones are marked to which construction materials are sent. For tissue building, the marking is done with DNA oligonucleotides that are held in place by chemical linking to a glass surface. Cells are the construction materials.

Each DNA oligo acts as biological Velcro to attach cells labeled with a specific DNA snippet, one that is complementary to DNA marking a zone. A cell's DNA snippet acts as a type of zip code directing the cell to its destination, says Gartner. Cells move around randomly, but they settle by DNA hybridization at their predetermined spot.

"DNA, in many ways, is like having many flavors of Velcro," says Gartner. The tissue is assembled by the addition of cells in multiple rounds, and the Velcro can also be used to place specific cells in certain layers, all of which offers flexibility for researchers, he says. Once assembly is complete, scientists transfer the tissue from the glass into a different material—a hydrogel that mimics the viscous, elastic extracellular matrix—and the tissue then grows in this new environment.

Stanford University chemist Carolyn Bertozzi calls Gartner a creative genius. His ideas seem like borderline science fiction at first, and then somehow he brings them to life, she says. His research program resembles no one else's; it is a unique reflection of someone who sees the chemical avenue for assembling tissues from cellular building blocks and giving them life. "If I called him a molecular Dr. Frankenstein, he would flash his silver surfer smile and consider it high praise," she says.

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Gartner completed his PhD work in chemistry at Harvard University and was a post-doctoral fellow in Bertozzi's lab, then at the University of California, Berkeley. Then he landed a professorship at UCSF, where he is happy to be, also because it is in his beloved San Francisco. Extensive travel has never yielded a better spot to live and work, he says. His phase on the East Coast, in Boston in particular, holds a special place in his heart, except for the heart zone devoted to surfing.

The eastern seaboard offers fine waves, says Gartner. But the flat spells are hard to bear. The waves eventually return, but by then lab obligations too often make him miss the swell. "It's nice to live in a place where the surf is consistently good and if you miss a day, you can always count on tomorrow," he says. "I also don't like tucking in my shirt."

When not in the lab, or surfing, Gartner enjoys cooking and spending time with his wife. "When I have free time on the weekends, I love to work in my garden, but the SF fog always conspires to foil my ambitions at horticulture."

Vivien Marx

Todhunter, M.E. *et al.* Programmed synthesis of three-dimensional tissues. *Nat. Methods* **12**, 975–981 (2015).