THE AUTHOR FILE

Jana Selent

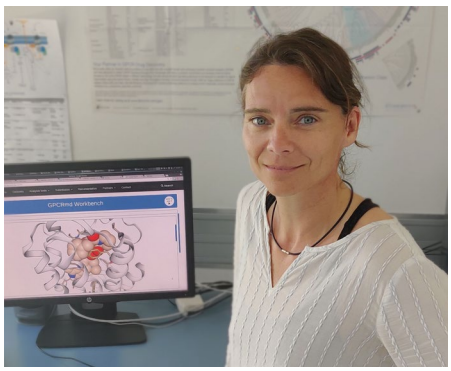
A platform for exploring GPCR secrets, powered by community, music and sports.

At Pompeu Fabra University in Barcelona, Jana Selent teaches. She also heads a lab, the GPCR Drug Discovery Group; holds a Miguel Servet research position at Hospital del Mar Medical Research Institute (IMIM), where she collaborates with physician-scientists; and, on occasion, strikes up projects with small biotech companies. A biomolecule that holds her fascination is the G protein-coupled receptor (GPCR), of which there are 800 types and different classes. In the world of drugs approved for use in people, these are the most frequently targeted receptors. What's fascinating about these membrane proteins, says Selent, is that beyond being gates to the cell they 'look' outward. Akin to antennae, they scour the world beyond the cell membrane for signals. Many receptors are quite specific in terms of the molecules they recognize and interact with, but over time researchers have shown, she says, that "they're actually very promiscuous."

It takes interdisciplinary approaches to explore the many secrets these well-studied GPCRs still have to impart, says Selent. This broad view might stem from her training as a pharmacist at Humboldt University of Berlin, which entailed immersion in biology, chemistry, analytical science and drug development. "I always wanted to know how things work in biology and the human body," she says. In her Humboldt training, later as a postdoctoral fellow at the University of British Columbia, in research stints at Martin Luther University in Germany, at the Leibniz Institute of Plant Biochemistry and then during her second postdoc at Pompeu Fabra in Spain, she strove for wet-lab and in silico lab training, such as in structural biology and bioinformatics. This kept nudging her "out of my comfort zone," which she enjoys.

When she began looking for GPCR labs, she found one at Pompeu Fabra, where she later joined the faculty. "Definitely better weather than in Germany," she says, where Selent is originally from. She's fluent in several languages, and her preschool-age daughter is helping her mother hone her Catalan.

In her latest paper, Selent and colleagues in ten countries present GPCRmd, an online resource developed with the GPCR community. It's a web portal with datasets and software tools where people can tinker with molecular simulations. Labs with publicly available datasets can upload them into the portal and use tools to see their biomolecules from multiple angles and to simulate the movements associated with binding events.



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The idea for GPCRmd was born some years ago, but it takes public funding and wide community involvement to turn idea into reality and to keep things running. "With a community you are able to do these things," says Selent. She and her lab are heavily involved, as are other experts who help to curate and precompute simulations. "It's just fun working on it," she says. There's much exchange between her lab and other GPCR labs, which is good for her trainees. Such exchange is needed, given that each GPCR type has its peculiarities that affect simulations. When cells react to stimuli through their GPCRs, change happens in space and over time. "If you do a simulation you really follow the protein-dynamic behavior over time," she says.

Crystallographic data have atomic resolution but not temporal resolution. Protein crystallographers can fit GPCR models onto their electron density maps, but they would like to find more than one optimized point in conformational space. That's perhaps why they are big users of the platform, says Selent. Medicinal chemists use the platform to assess different interactions and binding locations and consider new molecules. Evolutionary biologists can use the resource to cluster proteins and "see how nature fine-tunes certain functions by sequence variability," she says. They might discover that receptors in distantly related species are quite similar. She hopes the resource can grow and help many labs and disciplines.

An IMIM server stores the resource's data, but computation is distributed through GPUGrid, which is headquartered at Pompeu Fabra. It's set up for molecular dynamics simulations with a network of volunteers who do graphics processing unit (GPU)-based computing. Simulations run faster on GPUs, says Selent. The set-up is similar to the protein-folding volunteer network Folding@home.

When she finds the time beyond family and work, Selent likes to hike, run and surf. "Any sports activity you can imagine, I love," she says. She also enjoys playing the piano, from the classics such as Chopin, Schumann and Mozart to jazz improvisation. Of late she has not played much. "Time will come again for that," she says.

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Some years ago, Selent invited Martha Sommer from Charité's Institute of Medical Physics and Biophysics to a conference in Barcelona. They have collaborated ever since, and they co-chair the European GPCR network ERNEST. Selent had predicted how well their methods would complement one another, says Sommer: her experimental methods and Selent's computational approaches. "How could I say no to such a charming and down-to-earth woman?" says Sommer. At the time, Selent was well established in GPCR molecular dynamics, and "I was amazed at how adeptly she 'caught on' to my protein of interest, the GPCR-regulatory protein arrestin, and her intuitive sense of how biomolecules work," says Sommer. She and many others "have benefitted immensely from Jana's natural talent, her openness and honesty, and her disarming personality that brings out the best in everyone around her." ❐

Vivien Marx

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Reference
Rodríguez-Espigares, I. et al. GPCRmd uncovers the dynamics of the 3D-GPCRome *Nat. Methods* https://doi.org/10.1038/s41592-020-0884-y (2020).