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Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
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Dear Dr. Brun:

I write to strongly support the application of Dr. Gonehal Venugopala Reddy (Dr. Venugopala Gonehal as it is on some of his official U.S. documents, which translate the name order of south India differently than Venu himself does) for a faculty position. Venu has been a postdoctoral scholar, and then a senior postdoctoral fellow (a faculty position) in my laboratory at Caltech since June, 1999, a total so far of six years and change. He came to my lab from the Tata Institute in Mumbai, India, the premier graduate school in biological sciences in that large country. As a graduate student he worked on cell-cell signaling and differentiation in the cells of developing *Drosophila* mechanoreceptors. Venu arrived in my lab very highly recommended by his graduate school mentors, and by the other *Drosophila* geneticists he had worked with, in Europe and in India. His graduate advisor, Veronica Rodrigues, wrote that "Venu is clearly the best Ph.D. student to graduate from my laboratory and is clearly among the top 5% of about 60 doctoral students our department has produced over the last fifteen years..." As this is the best department in India, that is an impressive recommendation. Vijay Raghavan, head of the Tata Institute's National Centre for Biological Sciences in Bangalore (and a former postdoc in my lab, and therefore familiar with Caltech), wrote that "Venu is in the class of Raffi Aroian, Paul Garrity, Mark Running, John Bowman, John Ng and Stuart Kim" - in other words, comparable to top Caltech students of the past two decades. He added that "Venu is a solid and top class intellect," and also, that he "has a fine sense of humour and is a great lab person..." Pat Simpson, a French *Drosophila* geneticist in whose lab Venu spent three months in 1997, wrote "I was very impressed by him. He is very quick, knows the literature extremely well and seems to have accomplished an amazing amount..."

All of the accolades from his Drosophila colleagues turned out to be deserved. In my laboratory, where we work on plants and the development of *Arabidopsis thaliana* flowers and shoots, Venu started out to study the shoot apical meristem (the growing tip of a shoot) at a new level. For years we and others had made mutant plants, selected those that had meristematic abnormalities such as meristems that are larger than normal, and then cloned and characterized the genes. In the course of this work we learned that

the cells at the tip of the meristem, the central zone cells, make a secreted protein (CLAVATA3) that appears to be the ligand of a receptor kinase (CLAVATA1) expressed in the cells below the central zone (the cells of the rib meristem). Signaling from the central zone to the rib meristem either reduces the rate of division of the rib meristem cells, or increases their rate of differentiation (or both), thereby having the effect of reducing the size of the rib meristem. Signaling from the rib meristem to the central zone (via a gene studied most in the laboratory of Thomas Laux in Germany, a homeodomain family member called *WUSCHEL*) enlarges the central zone – perhaps by causing respecification of cells from the surrounding peripheral zone to central zone fate, or perhaps by causing the central zone cells to divide more rapidly. To settle the questions of how *CLAVATA1* and *WUSCHEL* really act on shoot meristem cells (division or differentiation?), we had to look at the effects of changing signaling through the CLAVATA pathway while we were watching the meristems, rather than trying, as before, to infer the immediate effect by looking at mature meristems that had lacked the function, or had ectopic function, of the signaling components since fertilization. To do this we needed to accomplish three tasks. First was to develop a method for live imaging of growing shoot apical meristems. Next was to make transgenic plants that showed the domains of the meristem (such as the central zone) with fluorescent markers, so they could be recognized objectively in living material. Third was to develop methods to turn on and off the function of genes like *WUSCHEL* and *CLAVATA3* while we were watching, and then to record the immediate as well as the eventual effects on domains of gene expression, and on cell division behavior in the entire meristem.

Venu did all of this. He obtained and developed plants transgenic for fluorescent markers of nuclei and of plasma membranes, and developed (with another postdoc, Marcus Heisler) methods to observe these over a period of up to five days without injury, using a laser scanning confocal microscope. This was real *tour de force*, which allowed for the first time measurements of cell cycle time in all meristematic cells at once, and complete clonal analysis of the origins and divisions of cells in the meristem over the time when it produced multiple floral primordia on its flanks. Venu was able to derive a variety of novel conclusions about cell division in shoot apical meristems and on the role of oriented cell division in the formation of flower primordia. These were published as Reddy, G.V., Heisler, M.G., Ehrhardt, D.W. and Meyerowitz, E.M. (2004) Real-time analysis reveals oriented cell divisions associated with morphogenesis at the shoot apex of *Arabidopsis thaliana*, Development **131**, 4225-4237.

Venu then used addition fluorescent markers (different colors of GFP) to mark gene expression domains, including those of *CLAVATA3* and *WUSCHEL*, in the meristem. And then he added to this control of *WUSCHEL* (he activates it by fusing to a rat glucocorticoid receptor steroid binding domain, which holds it inactive in the cytoplasm until a human glucocorticoid is added to the plants); and control of *CLAVATA3* (activated using a steroid-activated promoter, inactivated by inducible RNAi). The first part of this part of the project, following the effects of turning off *CLV3* function on meristem cell division, and on the size of the central zone, has just been published as Reddy, G.V. and Meyerowitz, E.M. (2005) Stem-Cell Homeostasis and Growth Dynamics Can Be Uncoupled in the *Arabidopsis* Shoot Apex, Science **310**, 663-667.

Venu is accumulating data on *WUSCHEL* expression when CLV3 is inactivated, and has constructs for activating *WUSCHEL* and following the results in real time, thus I expect additional papers, with a similar impact to the earlier ones.

In summary, Venu has taken on an extraordinarily hard set of problems, both conceptual and technical, and has triumphed, with the result that he has a set of new methods that put him in a position for years of profound analysis of plant growth.

He has also been a participant in our discussions with collaborators on computational modeling of the cellular interactions in the shoot apical meristem, discussions that have resulted in recent publications (of symposium presentations) that include Venu as a co-author: Gor, V., Shapiro, B.E., Jönsson, H., Heisler, M., Reddy, G.V., Meyerowitz, E.M. and Mjolsness, E. (2005) A software architecture for developmental modeling in plants: The Computable Plant project. In R. Hofestaedt and N. Kolchanov (Eds.) Bioinformatics of Genome Regulation and Structure II, Kluwer, Boston, pp. 345-354; and Jönsson, H., Heisler, M., Reddy, G.V., Agrawal, V., Gor, V., Shapiro, B. E., Mjolsness, E. and Meyerowitz, E. M. (2005) Modeling the organization of the WUSCHEL expression domain in the shoot apical meristem. Bioinformatics **21**, suppl. **1** i232-i240.

In person he is delightful – very quiet certainly, but a lucid participant in discussions, a thoughtful speaker, and an able collaborator. An example of this is his working with other postdocs in my lab on the analysis of the function of new gene that acts in leaf development (Ohno, C., Reddy, G.V., Heisler, M. and Meyerowitz, E.M. (2004) The Arabidopsis JAGGED gene encodes a zinc finger protein that promotes leaf tissue development. Development **131**, 1111-1122). He has also served very successfully as mentor for Caltech undergraduate students in our summer SURF program (Paul Nagami and Emma Thomas) and as the mentor for a visiting student from Germany, Stephan Wenkel. Thus he works well with others, and is an experienced supervisor of students. He has done extraordinary work here, and is facing a bright future at the interface of plant genetics, development, and novel optical methods.

Sincerely,

Elliot Meyerowitz