THE SCRIPPS RESEARCH INSTITUTE

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Biocomplexity Faculty Search Committee
c/o Prof. Rob de Ruyter van Steveninck
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Dear Biocomplexity Faculty Search Committee Members:

I am delighted to write a letter on behalf of Qihong Huang. Qihong joined my lab at Scripps approximately two years ago as we were developing a functional genomics focus in the group. He has played a major role in these efforts and has initiated (largely on his own) a number of very exciting projects in cell based phenotypic/pathway screening and in forward mouse genetics. He is among the best of an outstanding group of coworkers in my lab.

Utilizing an arrayed matrix of approximately 20,000 cDNAs, Qihong has carried out a gain-of-function cellular screen to elucidate proteins involved in the modulation of p53 transcriptional activity. In addition to identifying 9 novel regulators of p53 in mammalian cells, Qihong demonstrated that the basic helix-loop-helix (bHLH) proteins HEY1, HES1 and AP-4 activate p53 through repression of hDM2 transcription. Ectopic expression of these bHLH transcription factors in both zebrafish and avian developmental systems resulted in a phenotype of p53 overexpression. Furthermore, Qihong has shown that Ras and Myc mediated transformation of mouse embryonic fibroblasts (MEFs) was abrogated by expression of HEY1 in a p53-dependent manner. These results show that these transcriptional inhibitors are members of an evolutionary conserved network which governs p53 function. Most recently, Qihong has carried out a small molecule screen of roughly 100,000 molecules and identified several molecules that are selectively cytotoxic to HCT116 p53-/- cells versus HCT116 +/+ cells at submicromolar concentrations. Currently, we are investigating the mechanism of action of these molecules, which appear to be selective kinase inhibitors.

Qihong has also carried out cellular screens in yeast to identify novel checkpoint genes. He screened the collection of all homozygous yeast deletion strains for nocodazole sensitivity in order to identify novel genes involved in the mitotic checkpoint. Using this genomic approach, several novel mutants sensitive to antimicrotubule agents were identified. One of the mutants contains a deletion of the *RTS1* gene, which codes for a regulatory subunit of protein phosphatase 2A (PP2A). Through a series of biochemical assays Qihong demonstrated that Rts1p plays a critical role in regulating the mitotic checkpoint and is similar in this aspect to the other PP2A regulatory subunit Cdc55p.

Qihong has also initiated a very exciting project in forward mouse genetics that exploits the recessive ENU screen we set up at GNF. In order to discover cancer-resistant genes, Qihong screened a collection of ENU-induced mutation mice for resistance to transplanted tumors. Using this forward-genetic approach, he identified 4 mutant mice that are resistant to tumor formation when injected with syngeneic transformed cells (the screen has 100% penetrance in a control nonmutagenized population). Mapping of the mutant genes in these mice is underway. These mouse models will help to elucidate

the cellular and genetic mechanisms of host resistance to tumor development.

As you can see, Qihong has been highly productive in my lab. He has initiated three exciting projects, which are yielding very interesting and significant results. Qihong functions independently in the lab and is more like a colleague than a postdoctoral fellow (in addition to his own efforts he is guiding a first year graduate student in genomic studies of Runx3 function). He is very bright, has a terrific work ethic, is an outstanding experimentalist and has excellent knowledge of the literature. His proposals are exciting and significant, and exploit the foundation he has laid here. Qihong's communication skills are good and he should have no problem in teaching or writing grants.

In conclusion, Qihong is an outstanding candidate for a tenure track position. He has already played a major role in creating our "genomics" program and will no doubt establish an exciting research program. I enthusiastically recommend him to you.

Sincerely,

Peter G. Schultz
Professor, Department of Chemistry
The Scripps Research Institute
and
Director, Genomics Institute of the
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