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Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology, Indiana University
Jordan Hall 142, 1001 E 3rd Street
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RE: Arina Omer

Dear Committee Members:

I am delighted to recommend Dr. Arina D. Omer for your open Assistant Professor position. I rank Arina with the best young scientists I have known over the past 30 years as a professor. She's very bright, is an exceptional scientist and has terrific teaching potential. The research she performed for her Ph.D. and extended as a postdoctoral fellow is truly outstanding. This body of work includes not one, but two landmark discoveries in RNA science – one is a major finding in evolutionary biology and the other an important breakthrough in cell-free biochemistry. In her most recent work, she continued to push the frontier further, by helping discover many new small non-coding RNAs in the Archaea. I will dwell primarily on the earlier work and say only a little about the newest, unpublished work.

The bulk of Arina's doctoral and postdoctoral research was in the burgeoning field of small nucleolar RNAs (snoRNAs) and snoRNA-protein complexes (snoRNPs or 'snorps'). Nucleoli contain scores of these RNAs/RNPs and these have recently been determined to play essential roles in the maturation of ribosomal RNA (rRNA). Most snoRNPs mediate the formation of modified nucleotides in rRNA (and other RNAs), and a few are involved in processing (cleavage) of the large precursor rRNA transcripts. The modifying snoRNPs are of two types, defined by structure and function and one type was the centerpiece in Arina's work. This class of snoRNP creates methylated nucleotides, by addition of a methyl group to the ribose sugar of the RNA chain (yielding a 2'-O-methylated nucleotide). These are called the box C/D snoRNPs, named for short conserved sequences in the snoRNA component. The other snoRNP-type modifies uridines in rRNA. These snoRNPs can be viewed as rRNA-modifying machines on an assembly line that produces ribosomes.

My own laboratory works in this field – on yeast snoRNPs and rRNA biosynthesis, and I have followed Arina's work very closely over the entire course of her time in Pat Dennis' (top notch) laboratory. I have come to know Arina well personally too, through lengthy

discussions at scientific meetings. In addition, I have observed her give formal talks at several international meetings and discuss her work informally in small groups.

Arina is lead author on two seminal papers. One paper (in *Science*) describes the discovery of orthologs of the eukaryotic methylation guide snoRNAs in the Archaeal kingdom; the RNAs are called sRNAs. The other paper (in *PNAS*) reports the first success in achieving RNA-guided methylation in a cell-free system, using RNP methylation complexes reconstituted *in vitro*.

The methyl guide RNAs in the Archaea were discovered by sequence analysis of small RNAs immunoprecipitated with antibodies specific for a candidate s(no)RNP core protein (called fibrillarin). That analysis revealed the presence of the elements that define a methyl guide RNA, i.e., boxes C and D, and guide sequences complementary to rRNA – and remarkably, to tRNA as well (this was a first). Subsequent analysis showed that methylation modifications indeed exist at the predicted sites in the two types of substrates. These findings were then extended to several additional Archaeal species, by genomic sequence analysis with collaborating computational biologists. These results showed the RNA-guided modification machinery is of ancient origin, and set the stage for Arina's second major paper. This exciting work was announced to the RNA community in a special talk at the annual meeting of the RNA Society.

In her second major paper, Arina was successful in establishing the very first *in vitro* system of RNA-guided methylation, from any source. Other laboratories had made progress in defining the early stages of snoRNP assembly in eukaryotic cells, however, Arina was the first to not only show the order of addition of the core proteins (to the guide RNA), but - magnificently, to demonstrate that the complexes made of Archaeal components carry out methylation of a natural rRNA sequence. A new methyl group was added to the appropriate rRNA site in an accurate manner and with strong activity. Time has shown that it was brilliant to feature the Archaeal components, as there are fewer 'parts' and the parts are simpler. This is a very important development and opened the way for defining the chemical and structural basis of this unusual process. It is important to realize that this mechanism represents a completely new paradigm in RNA science - there is no other like it. Methylation modifications in RNA have long been known in the Bacterial kingdom; however, it seems clear these are created by 'conventional' enzymes, without a guide RNA co-factor.

Arina's current work involves discovery and characterization of additional new species of non-coding small RNAs in Archaea. She was one of the first to start systematic exploration for such species and one of the first to succeed. Characterizing the functions of these new species will keep her busy for a long time and the potential for continuing to make important new breakthroughs seems high.

Arina has a terrific mind, an enormous love of science and she is a wonderful experimentalist. Her presentations and interactions with others are a pleasure to observe. She has poise and confidence that I found unusual for a person at an early stage (or any stage, for that matter!). At international meetings I have seen her challenged with difficult

questions by senior scientists, including competitors, and she answers in a clear and complete manner that is both at-ease and professional. She loves her work and wants others to share the excitement. In my view, she has all the key qualities to excel as a teacher, as well as a research scientist. Importantly, Arina is a 'people person' and will be an excellent departmental and university colleague.

In summary, Arina Omer is a first rate young scientist with outstanding potential for the future. I think she is a wonderful candidate.

Sincerely,

A handwritten signature in black ink, appearing to read "Maurille J. Fournier". The signature is written in a cursive style with a large, prominent initial 'M'.

Maurille J. Fournier, Ph.D.
Professor Emeritus