



Photo Courtesy of Maja Bucan

Maja Bucan, Ph.D.

Maja Bucan received her B.S. in Molecular Biology and Physiology and her Ph.D. in Biology from Belgrade University, Yugoslavia. She completed her post-doctoral fellowship at the Imperial Cancer Research Fund in London and the Wistar Institute in Philadelphia. As Professor of Genetics in the Penn Department of Genetics, she works on identifying the genetic basis of psychological and behavioral disorders. Dr. Bucan is also the Interim Director of the Penn Center for Bioinformatics and the Chair of the Genomics and Computational Biology Graduate Group.

What are your current research interests?

I am interested in the biological basis for behavior. I am especially interested in genes that cause susceptibility to psychiatric disorders. There are two reasons: I am interested in everything related to the brain, but I am also fascinated by the fact that these disorders are so common. I worked as a postdoctoral researcher on Huntington's. It is a striking, devastating disease. I see unbelievable need to work on a disease that is common, because if I contribute, I could potentially affect the lives of many individuals and children.

Can you describe why you study endophenotypes?

The endophenotype is not a disease, but it is a component of the disease. "Phenotype," like "disease" is a big umbrella, but now you can look at the phenotype, or clinical manifestation, and divide it into individual components. For instance, in autism, there is a major problem in social interactions and repetitive behavior. But many individuals who have autism also have anomalous sleep patterns and language delay. So instead of doing genetics in children with autism and their siblings who do not have autism, you can use endophenotypes to do genetics. You can realize that an autistic child has delayed language, but his brother or sister also has delayed language, so maybe there are genes responsible for delayed language. Since autism is polygenic, maybe in the autistic child, there is a combination of genes that is different from the non-affected child, but even the non-affected child

inherits some of the susceptibility losses.

Are some endophenotypes, like sleep disruption, common in other diseases?

Yes, this is extremely important. There is a lot of effort to find what is specific to each disease. In my view, and this is based on studies in the mouse, there will be a set of genes common in many diseases. I think that by finding this set

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of common genes, it will be easier to find the specific aspects of each disease.

In my own work, one of my mice had a mutation in a gene involved in synaptic transmission. We could see that in combination with different strains, the phenotypes were changing. You can have circadian anomalies in one crossing, and another phenotype in other crossings. All of these mice have the same mutated gene, but the manifestation is different due to other interacting genes. So, the important message is that we cannot work on one gene at a time. We must make an effort to know entire pathways or networks of genes, and then look at their inheritance.

This is the meaning of the study of genomics, correct?

Exactly. What we are now doing in studies with psychiatric disorders is determining the genetic architecture, or the genomic landscape. We are looking at each individual to determine a set of genes that are changed.

What are some future applications of genomics?

There is something in the research that I am doing right now that has major implications for the future. During the last year I have been working with colleagues in the Center for Applied Genomics at the Children's Hospital [of Philadelphia]. We were able to establish high density genotype maps for many individuals, mostly with autism, but also some with bipolar disorder. We are also looking into a genome with many controls, or healthy individuals. We know that the genome of each individual is very unique. There are more differences between brothers and sisters or parents and children than we originally expected. It turns out our genome has small duplications and deletions everywhere. This means that in treatment of different diseases it will be very important to know the genetic make-up before selecting individual treatments.

Personalized medicine is coming, in my view, much sooner than we thought. Several years ago, we felt that it might come in 10-15 years from now, but it is literally around the corner. With high-density genotyping arrays, we are learning much more about our genome. Also, these new methodologies are telling us why we had so many problems finding susceptibility losses before.

What is the biggest challenge in your research?

That is very easy. The biggest challenge right now is definitely research funding...there is a problem because only a very small portion of grants are being funded and there are many brilliant experiments that are not being done. That is the greatest challenge.

More generally, there is a need to juggle many things. We must juggle the educational aspect of our work, the research aspect, and many other aspects of the field. There are lots of reviewing grants, reviewing papers etc.

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How will advances in computing affect computational biology?

The most informative experiments are experiments done on an incredibly large scale. Also, we are now encouraged to share our data. So even undergraduates, even high school students, can start experiments based on data that is already published. By mining data that is already available, you can develop hypotheses and then test them experimentally in the laboratory. You are not starting with experiments, you are starting by analyzing what's already out there. That is important.

Computational biology has exploded, and we at Penn are on the forefront. In the early 1990s, my colleagues set up undergraduate programs in computational biology. As a biology major, you can have computational biology as a concentration, and as a computer science major you can focus on computational biology. We also have a computational biology graduate group, and I am the chair of that group.

What contributions have undergraduates made to your research?

They have made a tremendous contribution. The main reason is that in our work we have experiments that must be

done...but there are other findings that are maybe too risky for a postdoc or student. These side-branches are exploratory work that needs to be done, and they can be done by undergraduates. I am also aware that it is difficult for undergraduates to come into the lab saying, “This is what I want to do,” because my work is very different. We do studies in behavior in mice, computational biology, and molecular biology. In my view, undergraduates should work with different individuals for the first few weeks, and then by getting exposed to different aspects and experiments, they will find what is the most interesting to them.

What advice do you give your undergraduates who want to pursue careers in science? How can they advance their goals?

My first advice is not to jump from one lab to another. It is always possible to choose a lab where you can address the same problem using different methods. For instance, when students want to do senior theses in my lab, I always tell them to work first during the summer, because they will have a lot of time and they can make some major advances. Then they can start their senior thesis. It is always advantageous to work on the same project for a long period of time.

— Interviewed by Evan Daugharthy