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Research Profile
Dr. Boriana Marintcheva and Protein Synthesis

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“Modern science has been a voyage into the unknown, with a lesson in humility waiting at every stop,” late astrophysicist Carl Sagan told us in an oft-quoted passage from his 1994 best-seller *Pale Blue Dot*. “Many passengers would rather have stayed home.”

Many perhaps would have, but not Bridgewater State virologist Boriana Marintcheva. Humility and determination, it seems, are two essential items in her professional toolkit and fuel for her own current voyage in modern science: finding out how to inhibit protein synthesis in human cancer cells. In Fall 2011, Dr. Marintcheva was awarded a CART Faculty and Librarian Research Grant to take the first steps in this ambitious project. To humility and determination, we might add *patience*: this Spring, Dr. Marintcheva took time to explain her research and teaching to this scientific layman.

“Cancer is a collection of many different diseases characterized by uncontrolled growth, such as we see in tumors and leukemia,” she explains. All cells are built from proteins. But these cells don’t follow the normal rules; they have a greater demand for proteins than normal cells and they divide non-stop. “Our line of thinking is this: if we can inhibit protein synthesis, cancer cells will be at a disadvantage.” This is similar in logic to the science on which radiation and chemotherapy is based, but those regimens are rooted in genetic information, not protein formation. Moreover, new cancer cells can be generated *because of* the damage caused by these routine treatments.

The novelty of Dr. Marintcheva’s work is that it targets protein behavior as it relates to synthesis of new proteins. More specifically, her work focuses on the unique properties of two proteins with “floppy tails” whose interactions are a weak link in protein synthesis. “If we can find a way to disrupt the bindings, then we can slow down the process of synthesis,” and, in turn, slow the growth of cancer cells in tumors. “It’s not a magic bullet,” she notes, “but it is a step on the road toward fighting the disease.”

Still, she admits, that’s a very long road. Scientific research applicable to abating cancer occupies scientists’ time and resources more than ever before, but their work is necessarily piecemeal and, often, disparate. “Everything is done in small steps,” Dr. Marintcheva notes, “and there is a lot of trial and error.” One running joke among scientists invokes etymology. “What we do is called re-search, because we have to search and search, again and again.”

Dr. Marintcheva’s project will begin in earnest this summer, when she undertakes her first task: to develop a framework or “assay” – a workable system, in her words – for testing chemical compounds to see if and how they interfere with protein synthesis. Her work will be done at the laboratories at Boston University, where her research collaborator (and husband), Dr. Assen Marintchev, works as a biologist at BU Medical School. Their collaboration is typical, in some ways, of the larger enterprise of scientific research. “No one researcher ever has all the equipment or expertise she needs,” she says. “We complement one another. That’s how the sciences work.” Their planned method is called *fluorescence polarization*: an approach that allows the researcher to monitor protein interaction by tagging protein tails, which makes visible and measurable their propensity to bind. “Once we know how nature behaves, we can move forward to the second step, which is performing the actual chemical screen.”

For Dr. Marintcheva, who has just completed her fourth year as a professor at BSU, the research presents a big
Overall Design of the Proposed Assay

This three-phase experiment tests the interaction of human proteins and the propensity of protein tails to bind and disrupt binding. In Phase A, a purified human protein, (eIF5B, or eukaryotic initiation factor 5B) depicted by a blue circle, is mixed with the tail of a second human protein (eIF5) indicated by the black curvy line, that is attached to a green fluorescent label (depicted with a green oval). The result of this is seen in Phase B: the interaction of eIF5B and eIF5 tail creates a stable complex (blue circle with attached black line and green oval). In Phase C, when the tail of a third human protein (eIF1A) depicted in the red curvy line is added to complex, the eIF1A (red) tail outcompetes the attached eIF5 (black) tail, thus disrupting the initially formed complex. In the described scenario, the molecule depicted by red wavy line acts to inhibit the expected protein interaction in A and B. Any small molecule that can mimic the action of the eIF1A tail disrupting the interaction between eIF5B and eIF5 would make a great candidate for an anti-cancer drug since it would be able to disrupt protein synthesis, thus slowing down cancer growth.