



Research Update

Meet Mohammed Saleem Bhat, PhD Vice Chair of Research Department of Surgery



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Mohammad Saleem Bhat, PhD, is the Vice Chair of Research in the Department of Surgery at Rush University Medical Center. He has been working in the field of prostate and pancreatic cancer research for the last 22 years. His research focus centers around the molecular pathology of cancer, therapeutics and disease model development. For the last 10 years, his laboratory has focused on the cancer health disparity field. He has published more than 60 peer-reviewed research articles and more than 40 conference articles. He joined Rush in February 2021.

Q. Can you give us an overview of the research you're doing at Rush?

A. I'm primarily focused on conducting research aimed at identifying biomarkers in the blood for the early detection of aggressive cancers, such as prostate cancer. My

research focuses on finding new tests to figure out the aggressiveness of the disease, as well as the likelihood the disease will recur.

I would like to stress that, unfortunately, such types of recurrent cancers remain untreatable because they appear at distant sites in body, such as in bone or the brain. I'm interested in finding new drugs and treatment strategies for such recurrent cancers. One aspect of my work that's important to me is to bring bench research to the bedside.

Q. What kinds of tests have you developed to identify those biomarkers?

A. What can happen with men who have prostate cancer is their cancer can go from treatable to untreatable, even with routine screening. We've come to understand that some kinds of prostate cancer hide within the body that aren't represented in the prostate-specific antigen (PSA) level. A patient will have normal PSA levels, then all of a sudden, their cancer has spread and there are no treatment options available for them.

I've discovered two kinds of proteins, S100A4 and BMI1, that are good indicators if a patient will relapse with their disease. If the levels for either protein are high, then it indicates a strong likelihood that the cancer is aggressive and will return. This is a very important development in prostate cancer treatment.

The BMI1 protein behaves like a stem cell protein, thus conferring a property of camouflaging to tumor cells, which help such cancerous cells to evade traditional therapy, such as radiation.

Then, after a certain period after the treatment is finished, these stem cell-like tumor cells regenerate and cause the cancer to metastasize to distant organs such as bones, the brain, liver or lungs.

The S100A4 protein works at different levels. When

the tumor is growing, the S100A4 protein starts accumulating within tumor cells as well as outside the tumor as secretory protein within the prostate gland. Levels of S100A4 proteins within gland that are too high cause some tumor cells to change their shape. These tumor cells thus remain unrecognized by the immune system. Thus, these cells escape quickly from the prostate gland and hide as mini or microtumors at distant sites. At a secondary level, S100A4 proteins secreted by microtumors help them to grow at bone sites and form as bone tumors in prostate cancer patients. Therefore, detecting both of these proteins, S100A4 and BMI1, early on would be an important step towards giving men with prostate cancer a real chance of getting through it. The good news is physicians can now use a non-invasive test to detect the presence of these proteins.

Q. The research you are doing also focuses on finding targeted therapies for prostate cancer. Can you elaborate?

A. Prostate cancer is a disease of several subtypes. If some of those subtypes are detected early, they can be treated successfully because they exhibit a protein called an androgen receptor. We already have effective therapies that target the androgen receptor.

On the contrary, there are some subtypes of prostate cancer, such as neuroendocrine cancer, or small cell carcinoma of the prostate whose development is not dependent on an androgen receptor. As a result, they can't be treated.

My research is focused on investigating the causes of development of neuroendocrine prostate cancer in men so that appropriate drugs can be discovered to treat it. I've found that the S100A4 protein drives neuroendocrine prostate cancer development. If we find the S100A4 protein in the blood, we know there are neuroendocrine cells somewhere in the body. Those cells won't be killed by conventional therapies.

S100A4 is abundantly present at micro-metastatic sites and neuroendocrine tumors in patients. We believe that tumor-penetrating S100A4-specific therapies could be used as treatment as well as a drug-delivery tool to specifically locate micro as well as macro prostate tumors and kill them from within. We're currently developing a series of novel tumor-penetrating S100A4-specific antibodies and inhibitors which can also carry a payload of chemotherapies with them. One of the reasons I came to Rush was to start clinical trials of S100A4-targeting therapy

Q. An interesting and important focus on your work has been identifying the causes of underlying prostate cancer development and poor response to therapies with Black patients. What models have you developed to study the disease in this population?

A. We have a health disparity in that about 10% of Caucasian patients develop prostate cancer, while 13-14% of patients in the Black community develop it. Mortality is also high for prostate cancer in the African-American community. There are several studies that show there are genetic determinants for developing certain types of cancer. I am looking into the molecular, biologic and genetic factors that are the underlying causes of this disparity.

Right now, our models that study risk of developing prostate cancer are tilted towards Caucasian patients. There are one or two models for the Black community, but they don't represent the community at large. My research is focused on developing such models, which could be used to study causes of disease and the testing of new drugs specifically for Black patients. Our research has made several contributions in cancer disparity

in terms of identifying novel ethnicity-based discriminatory markers, established race-based 2D and 3D organoid models and race-based, patient-derived xenograft (PDX) models of prostate cancer.

Q. What drew you to Rush?

A. Both Rush and Chicago have vibrant cultures. I was also drawn to working with a diverse patient population here. I'm passionate about developing a model to help the Black community and Rush is the place to do it. I have always been actively involved in community outreach and philanthropy. In the past I've given lectures at local schools to foster scientific interest at local middle and high schools. I have also provided opportunities to students from underserved populations to visit my laboratory and receive training there. I enjoyed working on the program with BLACK100, a national association involved in promoting education and career development in Black students.

Q. Outside of your own research interests, you enjoy teaching and mentoring students. How do you see that role continuing here at Rush?

A. I have been passionate about teaching throughout my entire life. I started my teaching career as an elementary school teacher, then moved to middle and high school and ultimately taught students and researchers at the university level. I am invested in training the next generation of scientists in my laboratory. I enjoy fostering scientific acumen in students in underserved populations by offering them free summer training in my laboratory. I'm looking forward to continuing that at Rush.



Excellence is just the beginning.