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Gaining Insight into How Our Immune Cells Tune the Efficiency of Presenting Antigens

In treating autoimmune diseases and cancer, antigen presentation – a vital human immune process – is emerging as a cornerstone in treatment.

At Ryerson, Amra Saric, a PhD candidate in the department of <u>Molecular Science</u>, has undertaken exciting research here, providing further insight for scientists and physicians into how our immune cells tune the efficiency of presenting antigens.

Amra puts some of the process in lay terms. "When bacteria breach the physical barriers of our bodies, specialized white blood cells called phagocytes control the threat by consuming the pathogens in a process called phagocytosis (phago equals 'to eat')," she says. "The phagocytes also need to alert the body of infection to mount an appropriate response while also killing the bacteria for good. To do this, the cells transport the bacteria to small round organelles called lysosomes, the cells' stomach; a harsh, acidic environment filled with degrading enzymes. Despite these conditions, lysosomes must also preserve some of the smaller remnants of bacteria to deliver them to the surface of the cell in a process termed 'antigen presentation'."

Supervised by <u>Dr. Roberto Botelho</u>, Amra and her fellow researchers (Victoria E. Hipolito, Jason G. Kay, Johnathan Canton, and Dr. Costin Antonescu) identified a new role for a key molecule, called mTOR, which resides inside phagocytes. One function for mTOR was already known. As Amra explains, "mTOR is normally a metabolic sensor within cells that determines nutrient and energy levels in order to coordinate cell metabolism and survival."

However, Amra says the team made another remarkable discovery, namely that mTOR can also sense infection to modulate the architecture of entire cellular organelles. "mTOR," says Amra, "orchestrates connections between sensing bacteria and tubulating the lysosomal network. Without mTOR, phagocytes can no longer form lysosomal tubules which impairs their ability to present antigen."

As first author, Amra contributed to experiment design, conducted the experiments and documented the findings in a paper entitled "mTOR controls lysosome tubulation and antigen presentation in macrophages and dendritic cells." Her paper was recently published in <u>Molecular Biology of the Cell</u>.

Amra successfully defended her PhD thesis in January 2016. She has fond memories of her time at Ryerson noting the opportunity to work with "very talented and hard-working students" in her program, the support of her supervisor Dr. Botelho, and all the incredible opportunities she encountered at Ryerson: exposure to novel research, networking with scientists in the field – and travel. "I was fortunate enough to have attended six conferences throughout my graduate studies at Ryerson."

After graduation, Amra will pursue post-doctoral studies in the lab of <u>Dr. Juan Bonifacino</u> at the National Institutes of Health (NIH).

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