Researchers discover novel approach to stimulate immune cells

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Dipak Sarkar, professor in the Department of Animal Sciences at the Rutgers School of Environmental and Biological Sciences and his research team have been able to take a new pharmacological approach to activate the immune cells to prevent cancer growth through stimulation of the opiate receptors found on immune cells. Credit: Rutgers University

Researchers at Rutgers University have uncovered a new way to stimulate activity of immune cell opiate receptors, leading to efficient tumor cell clearance.

Dipak Sarkar, professor in the Department of Animal Sciences at the Rutgers School of Environmental and Biological Sciences and his research team have been able to take a new pharmacological approach to

activate the immune cells to prevent cancer growth through stimulation of the opiate receptors found on immune cells.

This work, featured on the cover of the May 11 issue of the Journal of Biological Chemistry, describes two structurally different but functionally similar opioid receptors, Mu- and Delta-opioid receptors. These receptors form protein complexes as either two structurally similar receptors as a homodimer—formed by two identical molecules—or two structurally dissimilar protein complexes as a heterodimer—formed by ethanol inducement—in immune cells. The team pharmacologically fooled these two structurally different but functionally similar opioid receptors to form more homodimers so that opioid peptide increases the immune cells' ability to kill tumor cells.

"The potential for this research can lead to production of endogenous opioids in the brain and the periphery becoming more effective in regulating stress and immune function," says Sarkar.

Opioids, like endorphins, communicate with the immune system, so when there is a deficit of endorphin – due to fetal alcohol exposure, alcoholism and drug abuse, anxiety, depression and chronic psychological stress – the body undergoes stress shocks and, as Sarkar suggests, causes "immune incompetence."

"Opioids act as the regulator of body stress mechanism, so when endorphins are low, body stress indicators are high," says Sarkar, who directs the Endocrine Research Program at Rutgers and is a faculty member of the Rutgers Center of Alcohol Studies.

"What's new about this latest research is that when we combine the Mu receptor blocker (antagonist) with the Delta receptor stimulator (agonist), the immune cells accrue increased foreign cell-killing ability," explains Sarkar. "This makes the body highly effective in fighting

against bacterial infection and tumor growth."

Sarkar believes that combining this opioid antagonist and agonist may have potential therapeutic value in humans for the treatment of immune incompetence, cancer, pain and ethanol-dependent diseases.

Previous research by the Sarkar group showed that replenishing endorphins by cell therapy did prevent many of the stress and immune problems in fetal alcohol-exposed test subjects. However, cell therapy is highly complex, involving the cumbersome process of producing endorphin cells from neural stem cells of patients and can sometimes result in rejection and other issues.

The beginning of the team's interest into how stress causes diseases started with the observation that mothers who suffer from alcohol abuse or with other developmental problems often give birth to children who exhibited hype-stress responses, linked to childhood disease, child abnormality, immune diseases and cancer.

As part of their investigation, the Sarkar research team learned that the endogenous opioid system in the brain is abnormal in kids and adults who demonstrate hyper-stress responses.

"With the link between hyper-stress responses and manifested immune issues, the goal has been to replenish the opioid deficit in the brain and lead to an effective therapy for immune and other diseases," explained Sarkar.

The team also found that when people consume alcohol, the effectiveness of the body's ability to defend against viral and bacterial invasion, and fight against cancer decreases.

"The overall goal of our research program is to increase our

understanding of and develop new therapy for the treatment of cancer, immune and other alcoholism-induced diseases," says Sarkar.

They hope that the promise of their novel pharmacological approach that modifies the activity of the opioid receptors of immune cells brings them one step closer in the long road to therapeutic advances.

Provided by Rutgers University