DNA component can stimulate and suppress the immune response

January 27 2009

A component of DNA that can both stimulate and suppress the immune system, depending on the dosage, may hold hope for treating cancer and infection, Medical College of Georgia researchers say.

Low levels of CpG increase inflammation, part of the body's way of eliminating invaders. But high doses block inflammation by increasing expression of the enzyme indoleamine 2,3 dioxygenase, or IDO, an immunosuppressor, the researchers say.

"The same therapy can have two different effects," says Rusty Johnson, a fifth-year M.D./Ph.D. student in the MCG Schools of Medicine and Graduate Studies. "It was assumed that giving this treatment at higher doses would cause more stimulation, but it has the opposite effect."

The researchers hope that manipulating the dosage can help them optimize the role of inflammation in fighting invaders such as tumors and harmful bacteria. Mr. Johnson presented the findings at the Midwinter Conference of Immunologists this month in Asilomar, Calif. He is working with Drs. Andrew Mellor and David Munn, co-directors of the School of Medicine Immuno Discovery Institute, who discovered IDO's immunosuppressive capabilities more than a decade ago.

With the help of Drs. Babak Baban and Phillip Chandler, scientists in MCG's Immunotherapy Center, they've also learned IDO inhibits inflammation by blocking production of interleukin 6, a secreted factor that causes inflammation.

"This suggests that IDO is a counter-regulatory mechanism that serves as a balance to prevent too much inflammation," Mr. Johnson says. "Too much inflammation leads to destruction of normal body tissue, and this shows IDO's importance in preventing this from occurring."

The researchers already knew that IDO protects tumors from the immune system. While working with collaborators Drs. Alex Muller and George Prendergast at the Lankenau Institute in Philadelphia, they learned its role in tumor formation.

"Without it, a mouse becomes resistant to skin tumor formation, and tumors that do form are smaller and less malignant," Mr. Johnson says.

They've also learned that the cells IDO uses to suppress the immune system - IDO-competent dendritic cells - originate from B cells, which produce antibodies to fight infection.

Source: Medical College of Georgia