Iron regulates the TLR4 inflammatory signaling pathway

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Iron is a micronutrient essential to the survival of both humans and disease-causing microbes. Changes in iron levels therefore affect the severity of infectious diseases. For example, individuals with mutations in their HFE gene have exceedingly high levels of iron in their liver and are more susceptible to infection with a number of microbes.

Exactly how changes in iron levels affect susceptibility to infectious disease has not been clearly determined, although it has been observed that mice lacking Hfe mount an impaired inflammatory response following oral infection with the bacterium that causes salmonella.

Bobby Cherayil and colleagues, at Massachusetts General Hospital, Charlestown, have now defined a molecular mechanism underlying the impaired inflammatory response to oral infection with the bacterium that causes salmonella in mice lacking Hfe.

Specifically, these mice have low levels of free iron in immune cells known as macrophages and this impairs signaling along a pathway required for sensing the presence of bacteria such as the one that causes salmonella and triggering an inflammatory response (the TLR4/TRAM/TRIF pathway).

As drugs that mimic the altered iron distribution associated with Hfe deficiency reduced intestinal damage associated with infection with the salmonella-causing bacterium and reduced intestinal damage in a noninfectious inflammatory situation, the authors suggest that local

manipulation of iron levels might provide a new approach to controlling inflammation.

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