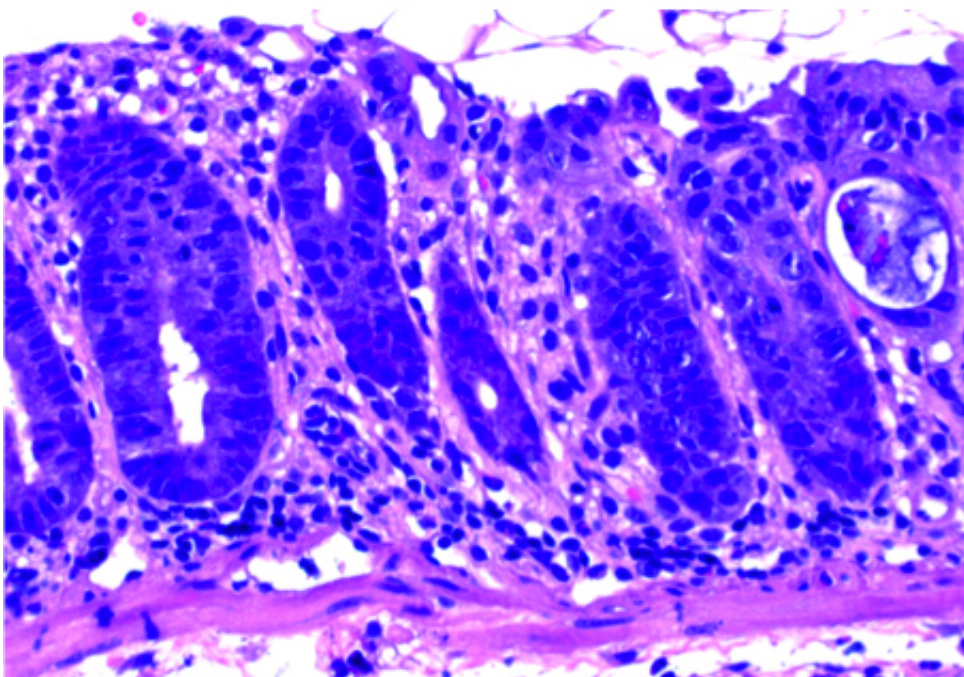
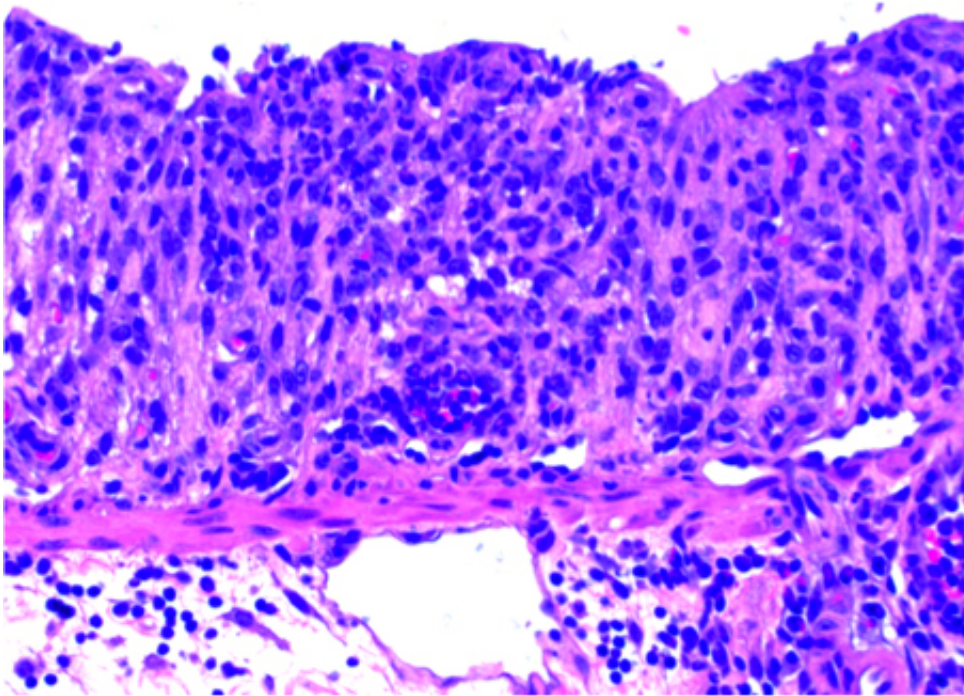


For a good gut feeling: Scientists explore molecular signals in inflammatory bowel disease

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The gut mucosa is not only responsible for the uptake of nutrients, but it also forms a barrier against the microbes that inhabit our intestine. If this barrier is broken, inflammation of the gut, colitis, develops. Upper graph (wildtype): By inducing experimental colitis, the mucosa structure is destroyed and a large infiltrate of inflammatory cells is present. Lower graph: Organisms lacking

transcription factor IRF9 are more resistant, seen by a more intact crypt structure and less inflammatory cells. Credit: MCB

Stress, an unhealthy diet and also the prolonged use of painkillers do not only upset the stomach, but are also associated with chronic colitis, an inflammatory bowel disease. A team led by Thomas Decker from the University of Vienna has now investigated one of the signaling pathways related to colitis in more detail. Their results underline the prospects of treatments currently under development and also indicate possible new therapeutic approaches. The study was recently published in the scientific journal *Molecular and Cellular Biology*.

Trillions of microorganisms colonize our gut and together form the intestinal flora that coats the inside of the intestine. The duties of these gut microorganisms are manifold: they digest food, produce nutrients, eliminate pollutants and interact with the human immune system. An imbalance in these microorganisms can cause abdominal pain, constipation or diarrhea. In the Western world an unhealthy diet, lack of exercise, stress and excessive use of antibiotics also lead to ever-increasing numbers of patients with chronic inflammatory bowel diseases such as colitis but also bowel cancer.

Chronic inflammatory bowel diseases and the role of interferons

Colitis - a [chronic inflammation](#) of the intestine - is treated with anti-inflammatory drugs. However, the signaling pathways involved in this inflammation are still not fully understood. New findings could therefore provide important cues for better or completely new treatment options. The team of Thomas Decker from the Max F. Perutz Laboratories (MFPL) of the University of Vienna has now studied the role of

interferons, a group of tissue hormones, in the development of colitis. "There are three types of interferons - our tests have shown that each type affects colitis differently. Type I interferons play a minor role, while type II interferons reinforce and type III interferons protect from the inflammation," explains Decker.

Surprising role of type II interferons

These first results triggered the interest of the scientists to find out exactly how the three interferon types mediate their different functions in colitis. Isabella Rauch, Postdoc and co- first author of the study, explains: "Our guess was that IRF9 would play a central role. This molecule transduces the signals of type I and III interferons, and therefore mediate the protective function of these interferons during the inflammatory response in colitis." Colleague and co-first author Felix Rosebrock adds: "However, what we found was that IRF9's main impact was not to transduce type I and III signals in colitis, but those of the type II interferons and thus to aggravate the inflammation." The researchers showed that the type II interferon signals cause the release of CXCL10, an attractant for cells that promote the inflammation.

New approaches for the treatment of colitis

The results of the study provide a new impetus for the treatment of colitis. They not only underpin the chances of success for a clinical trial of antibodies that inhibit the function of the attractant CXCL10, but also suggest that direct administration of type III interferons could protect patients from the inflammatory responses that trigger [colitis](#).

More information: Noncanonical effects of IRF9 in intestinal inflammation: more than type I and type III interferons. Isabella Rauch, Felix Rosebrock, Eva Hainzl, Susanne Heider, Andrea Majoros,

Sebastian Wienerroither, Birgit Strobl, Silvia Stockinger, Lukas Kenner, Mathias Mueller and Thomas Decker, in *Molecular and Cellular Biology*, 2015. DOI: [dx.doi.org/10.1128/MCB.01498-14](https://doi.org/10.1128/MCB.01498-14)

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