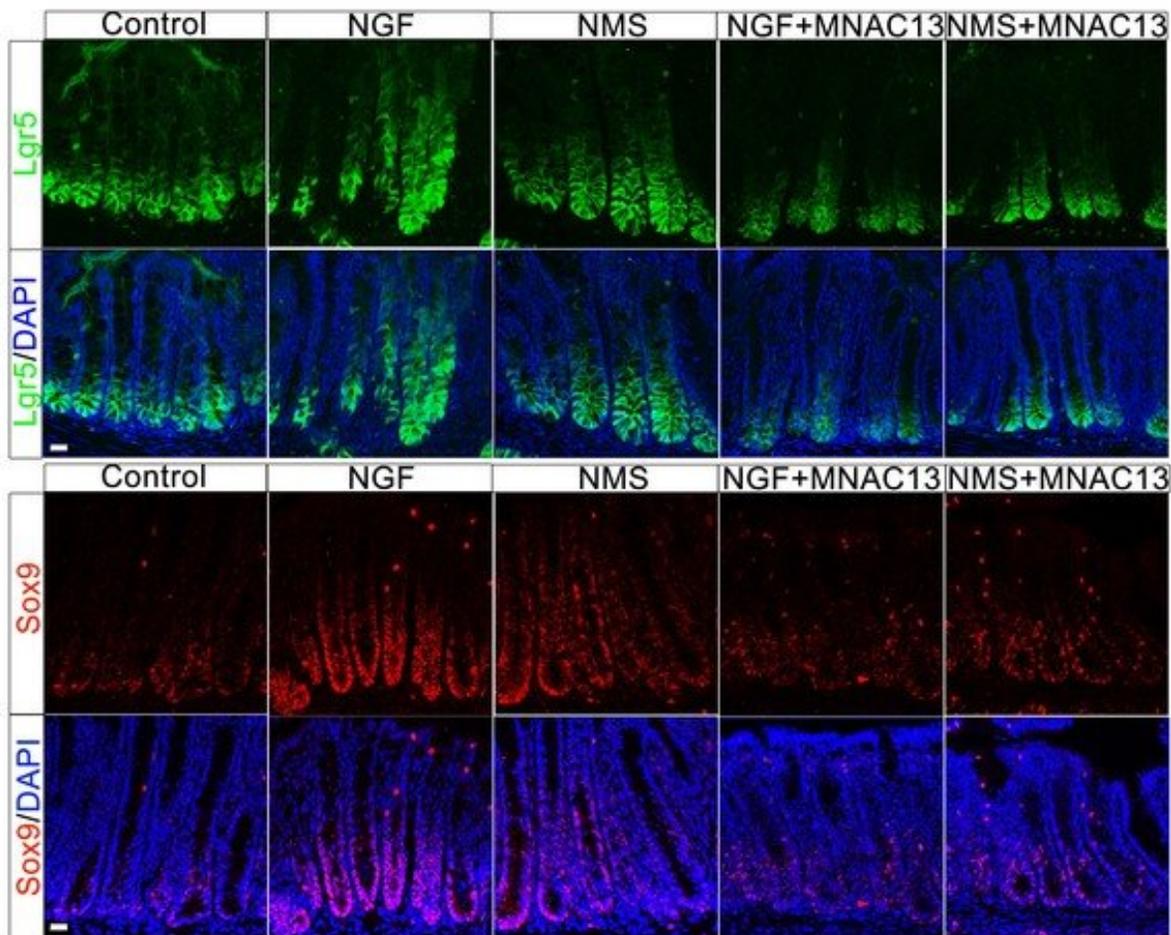


Researchers discover mechanisms underlying early life stress and irritable bowel syndrome

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Professor Bian Zhaoxiang and Dr Xavier Wong Hoi-leong find that Nerve Growth Factor is a key factor linking early life stress to the development of irritable bowel syndrome. Credit: HKBU

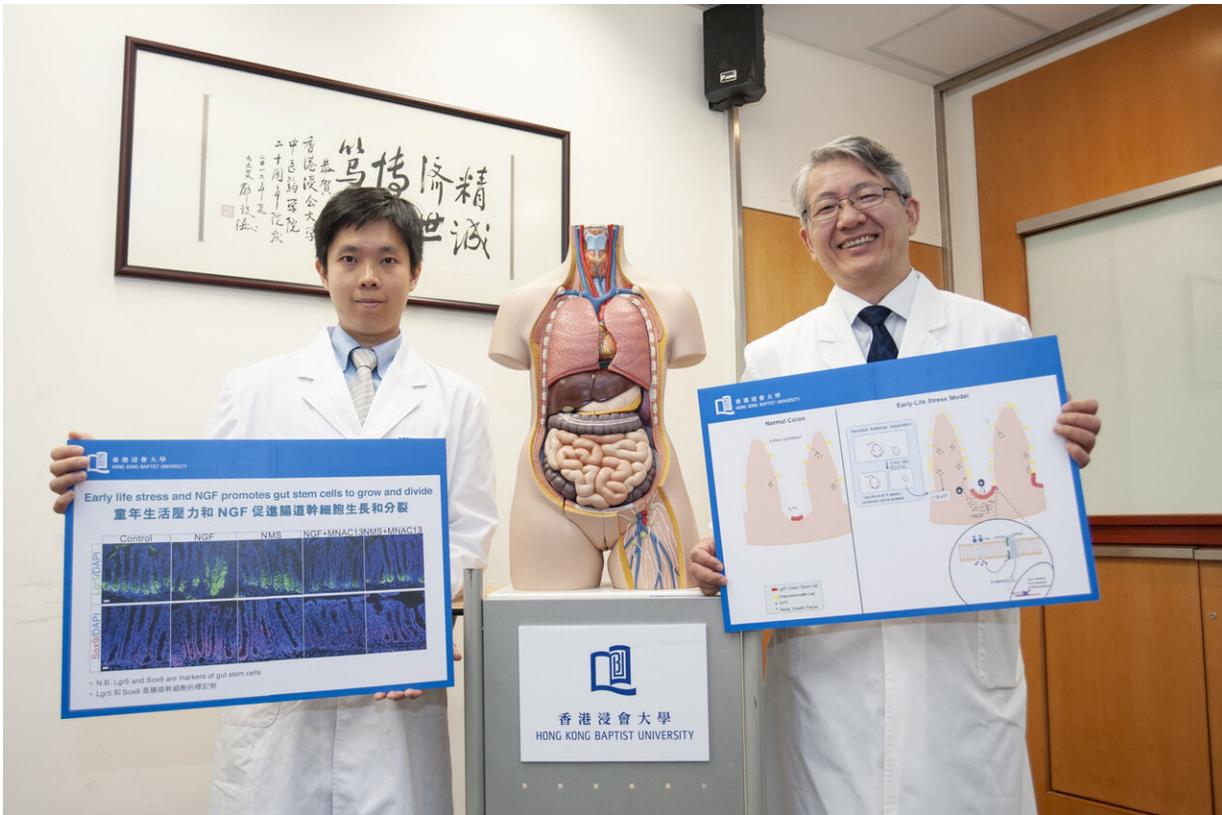
Researchers from the School of Chinese Medicine (SCM) at Hong Kong Baptist University (HKBU) have found that the abnormal rise of a soluble protein called Nerve Growth Factor is a key factor linking early life stress to the development of irritable bowel syndrome (IBS). The study, which is the first to demonstrate the link between traumatic psychological events occurring in childhood and lifelong health repercussions, could lead to the development of new treatments for gastrointestinal diseases.

IBS is a common functional bowel disorder characterized by stool irregularities, abdominal discomfort and bloating. While evidence increasingly links the impact of early life adversity with the development of IBS later on in life, the underlying mechanisms which translate a psychological event into gastrointestinal disease have remained elusive. This is especially pertinent since the disease in question, IBS, is widespread globally, including in Hong Kong. IBS presents a large health burden but there is currently no known cure. As a result, a better understanding of its development may present new ways to treat the disease.

The HKBU research team, which was led by SCM Chair Professor Bian Zhaoxiang and Research Assistant Professor Dr. Xavier Wong Hoi-leong, found that Nerve Growth Factor (NGF), a neurotrophic factor essential for neuronal development in the nervous system, was highly elevated in the gut of mice in response to early-life stress induced by neonatal maternal separation (NMS). This elicited IBS-like-symptoms in the animal model.

Regarding the mechanism, NGF acts on [intestinal stem cells](#) (ISCs) directly to promote their growth and proliferation. The significantly increased number of ISCs in the gut leads to abnormally high numbers of enterochromaffin (EC) cells, a type of intestinal cell responsible for serotonin secretion, which results in aberrantly high serotonin levels.

Aberrant serotonin production in the gut is known to cause IBS.



Early life stress and NGF promotes gut stem cells to grow and divide. Credit: HKBU

To uncover the mechanism by which early life stress alters intestinal homeostasis, the researchers set up an animal model of early life stress, known as NMS. They found that mice which experienced early-life stress went on to develop life-long IBS-like symptoms. In addition, the number of ISC and EC cells in the gut increased significantly by 50%. The animal model showed that the elevated secretion of serotonin, which is due to the increase in EC cell density in the gastrointestinal tract, triggered visceral hyperalgesia. This results in heightened pain in the

gastrointestinal tract, which is a hallmark of IBS.

To inhibit the activity of NGF, the team administered a specific NGF-blocking antibody into the animal model. This not only reduced ISCs and EC cell numbers, but also caused the IBS-like symptoms to completely disappear in the [animal model](#).

Importantly, they analyzed HKBU clinical data and found a significant positive correlation between NGF and serotonin in the sera of diarrhea-predominant IBS patients, NGF and serotonin increased by around 30% and 75% respectively in the IBS patients, compared with healthy ones, reinforcing the [causal link](#) between NGF and serotonin in the development of IBS.

The researchers concluded that NGF is a key driver of the development of IBS following early-life stress. Their work not only highlights the importance of NGF as a novel target in treating IBS, but also demonstrates that early-life adversity, such as a lack of parental care or abuse, may have serious lifelong health consequences. Their findings, entitled "Early life stress disrupts intestinal homeostasis via NGF-TrkA signaling", was published in the prestigious international journal *Nature Communications* (April 2019).

The team plans to continue to investigate the therapeutic potential of NGF-inhibitors as a treatment for IBS, including those found in Chinese medicine, and will strive to uncover the complete chain of events that link childhood [stress](#) to the [development](#) of IBS in adulthood.

More information: Hoi Leong Xavier Wong et al. Early life stress disrupts intestinal homeostasis via NGF-TrkA signaling, *Nature Communications* (2019). [DOI: 10.1038/s41467-019-09744-3](https://doi.org/10.1038/s41467-019-09744-3)

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