Study reveals why cancer anemia treatment leads to tumor growth

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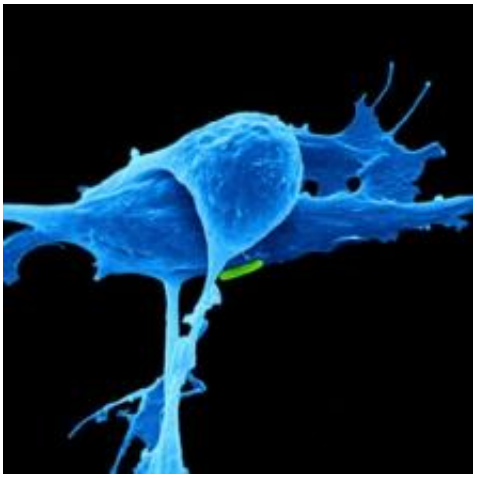

Scientists have shown why a drug widely used to treat chemotherapy-induced anemia in ovarian and breast cancer patients also may shorten survival times in some patients by inadvertently stimulating tumor growth.

Anil Sood, M.D., professor of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center, led a study that identified the cell receptor EphB4 as a catalyst for a chain of cell-signaling events leading to tumor growth. EphB4 is linked to the cancer anemia therapy known as recombinant human erythropoietin (rhEPO). Erythropoietins (Epos) are protein molecules crucial for red

blood cell production.

The study results were published in the Oct. 15 issue of *Cancer Cell*.

"Epos such as rhEPO has been used to relieve chemotherapy-induced anemia in cancer patients," said Sood. "Alarmingly, a growing number of studies have demonstrated that this treatment can compromise the overall survival of the patients."

Based on earlier studies including work done by Molecular Health of Heidelberg, Germany, scientists wondered whether the cell receptor known as EpoR which is normally associated with the anemia drug rhEPO, might be the cause. However, studies showed that EpoR "largely failed" to explain the effects of rhEPO on tumor growth.

"Evidence from other therapeutic areas has also suggested the existence of an alternative Epo receptor," said Sood. "Such observations, combined with a lack of convincing molecular explanation underlying the effects of rhEpo on cancer growth, prompted us to consider the existence of an alternative Epo receptor."

Sood's team revealed EphB4 as a trigger for downstream cell signaling that promotes rhEpo-induced tumor growth and progression. The researchers found that EphB4 enhanced tumor growth via STAT3, a protein or transcription factor vital to gene regulation. The investigation employed both in vivo and in vitro samples.

"The study showed EphB4 as a critical mediator of Epo-induced tumor progression," said Sood. "Our results have broad implications for understanding Epo biology."

The discovery of EphB4 as an alternative Epo receptor may open further investigation of how to stop tumor-stimulating effects of Epo-based

therapies. While additional validation studies might prove valuable in further defining Epo's adverse effects, the therapy remains an option for patients with chemotherapy-induced anemia, and patients are informed of possible side effects in advance of treatment.

Provided by University of Texas M. D. Anderson Cancer Center