Reducing the radioresistance of cancer

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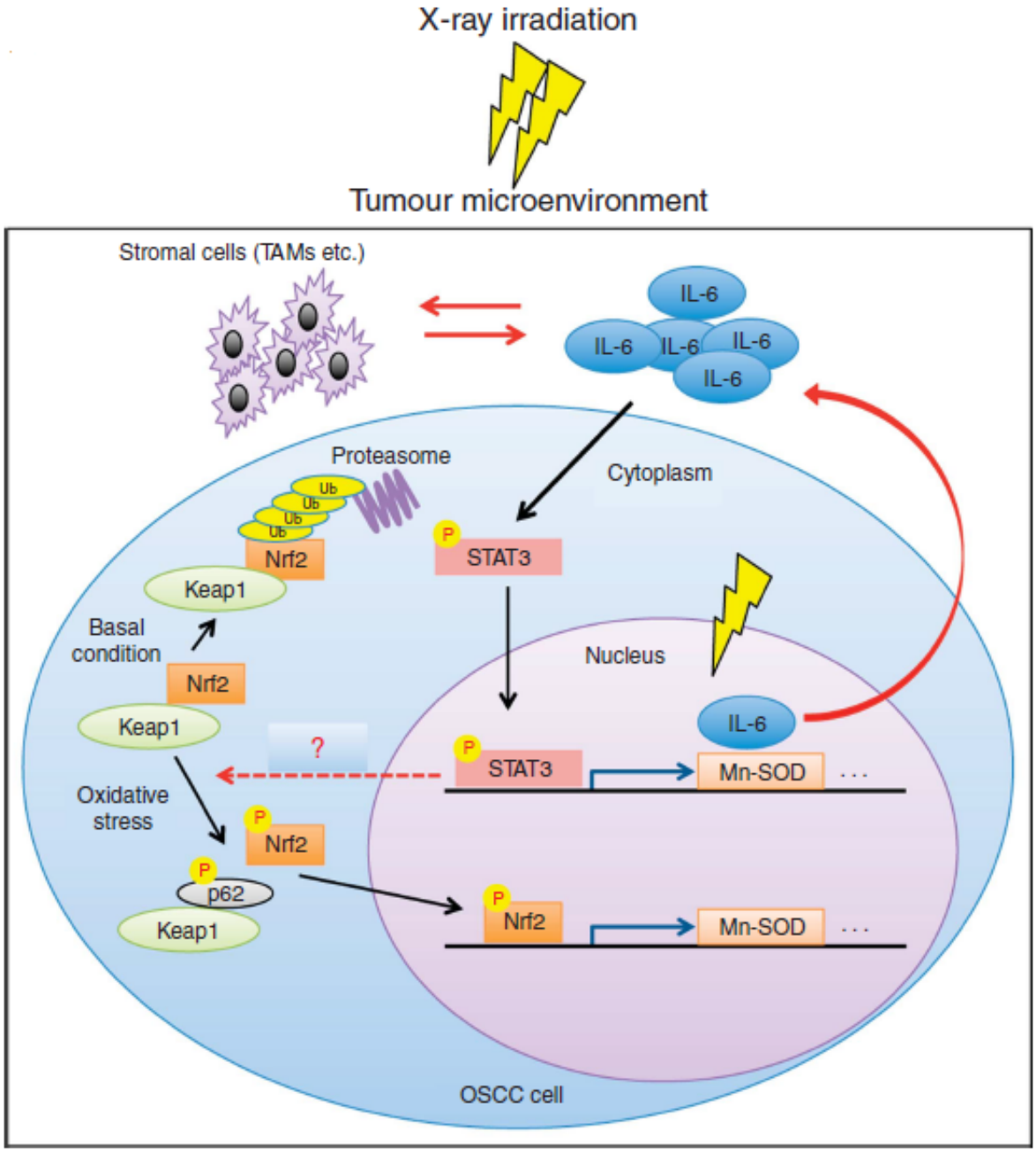

Kumamoto University (Japan) researchers revealed that when oral squamous cell carcinoma (OSCC) cells are exposed to X-ray irradiation, interleukin-6 levels increase and activate the Nrf2-antioxidant pathway. This leads to the production of antioxidants, such as Mn-SOD and IL-6, inside the nucleus and higher cancer cell radioresistance. Credit: Dr. Yuichiro Matsuoka & Dr. Hideki Nakayama, Adapted by permission from Macmillan Publishers Ltd on behalf of Cancer Research UK: *British Journal of Cancer* (Y. Matsuoka, et al., "IL-6 controls resistance to radiation by suppressing oxidative stress via the Nrf2-antioxidant pathway in oral squamous cell carcinoma," *British Journal of Cancer*, vol. 115, no. 10, pp. 1234-1244, 2016.), copyright 2016.

Most people recognize that many forms of cancer are treated with radiation therapy. However, some may not realize that there are cancer cells with the ability to survive this type of treatment. Oral squamous cell carcinoma (OSCC) is one of these forms of cancer, and is the reason why researchers from Kumamoto University in Japan began searching for methods to combat resistance to radiotherapy. Rather than going after the cancer cells directly, they attempted to find a way to control the biological mechanisms that aid in radioresistance. This meant looking at interleukin-6 (IL-6), a cytokine known for signaling the inflammatory response, and nuclear factor erythroid 2-related factor 2 (Nrf2), which is a protein that protects against oxidative stress.

Their approach consisted of multiple in vitro experiments on two different cancer cell samples. One sample was derived from tissue specimens taken from consenting patients with advanced OSCC who had undergone chemoradiotherapy (30 Gy total dosage). The other consisted of human OSCC cell lines which were obtained from the Japanese Collection of Research Bioresources Cell Bank (Osaka, Japan). These cells were irradiated with doses of either 6 or 10 Gy.

The results of the experiments provided evidence that IL-6 provides

protection from radiation therapy to cancer cells through interaction with the Nrf2-antioxidant pathway. "This interaction and the resulting protection from oxidative damage that we have discovered here is very interesting," said Professor Hideki Nakayama, one of the research group leaders. "As far as we know, we are the first to discover that IL-6 has such an effect on the Nrf2-antioxidant pathway. We hope new therapies that target IL-6 will give us an advantage over many types of radiation-resistant cancers."

The majority of the experiments performed were in vitro, which is a limitation of this study. However, research from the same group has already shown in a mouse model that the immunosuppressive drug tocilizumab, a drug currently used for rheumatoid arthritis, is effective against IL-6R as treatment for OSCC. Future research will attempt to expand on the researcher's idea of reducing the radiation resistance of cancer.

This research can be found in the *British Journal of Cancer*.

More information: Yuichiro Matsuoka et al, IL-6 controls resistance to radiation by suppressing oxidative stress via the Nrf2-antioxidant pathway in oral squamous cell carcinoma, *British Journal of Cancer* (2016). DOI: 10.1038/bjc.2016.327

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