TECHNOLOGY

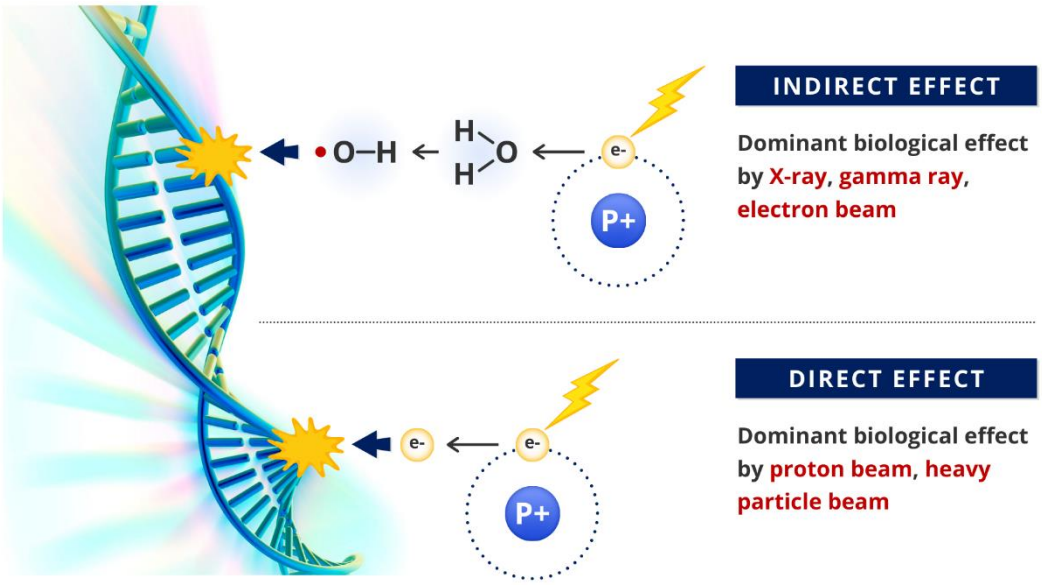
How KORTUC will change radio-resistant cancer to radio-sensitive

（https://vimeo.com/718151301）

Approximately 50% of all cancer patients will receive radiation therapy (RT) during the course of their illness. In most solid tumors, hypoxia occurs to some degree as a result of several factors, including the rapid growth rate of cancer cells and the highly disorganized/inefficient vasculature.

X-rays and electron beams are the main forms of radiation to treat cancer. Most of the damage is not caused by the radiation energy directly damaging tumor cells (Direct effect), but rather by the radiation energy creating highly reactive substances, especially so-called free radicals, that damage important structures in cells leading to cell death (Indirect effect).

Fig.1: Direct and Indirect Effects of radiation



The amount of oxygen inside a cell influences its susceptibility to radiation damage. Hypoxia (low oxygen levels) make cells more resistant.

New radiosensitizer, KORTUC, overcomes this problem. KORTUC contains 3% hydrogen peroxide (H_2O_2) and 1% sodium hyaluronate. H_2O_2 is the active ingredient for this radiosensitizer and is the only agent known to be capable of inactivating antioxidative enzymes and producing an excess amount of H_2O_2 to induce lysosomal membrane instability leading to apoptosis (H_2O_2 effect). Sodium hyaluronate delays decomosition of H_2O_2 and maintains a high partial pressure of oxygen in the tumor up to at least 24 hours following an intratumoral injection of the KORTUC as well as exerts the effect of mild pain killer at the injection site.

Fig. 2: The importance of KORTUC in neutralizing enzymes that protect tumor cells

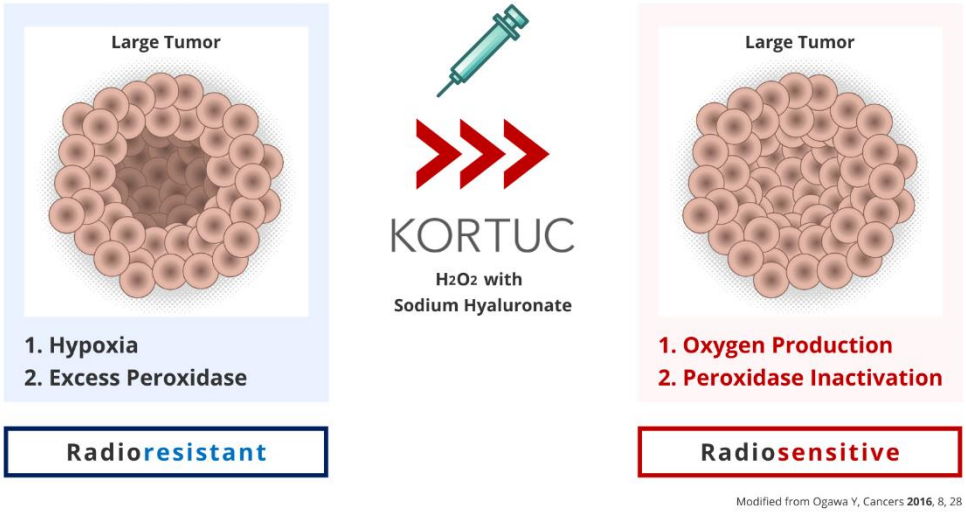
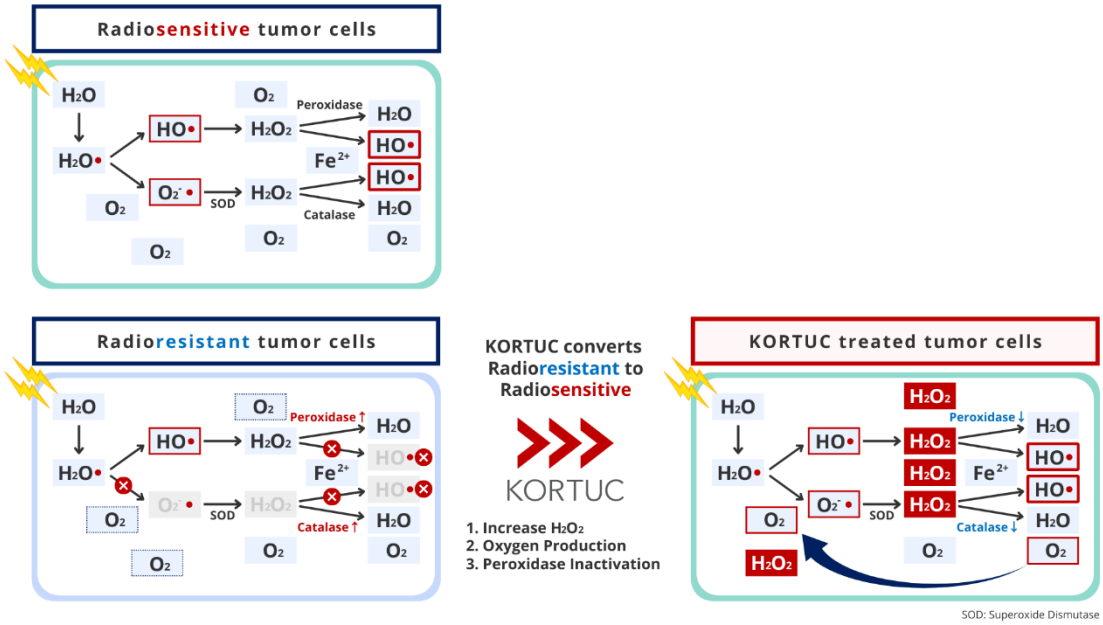


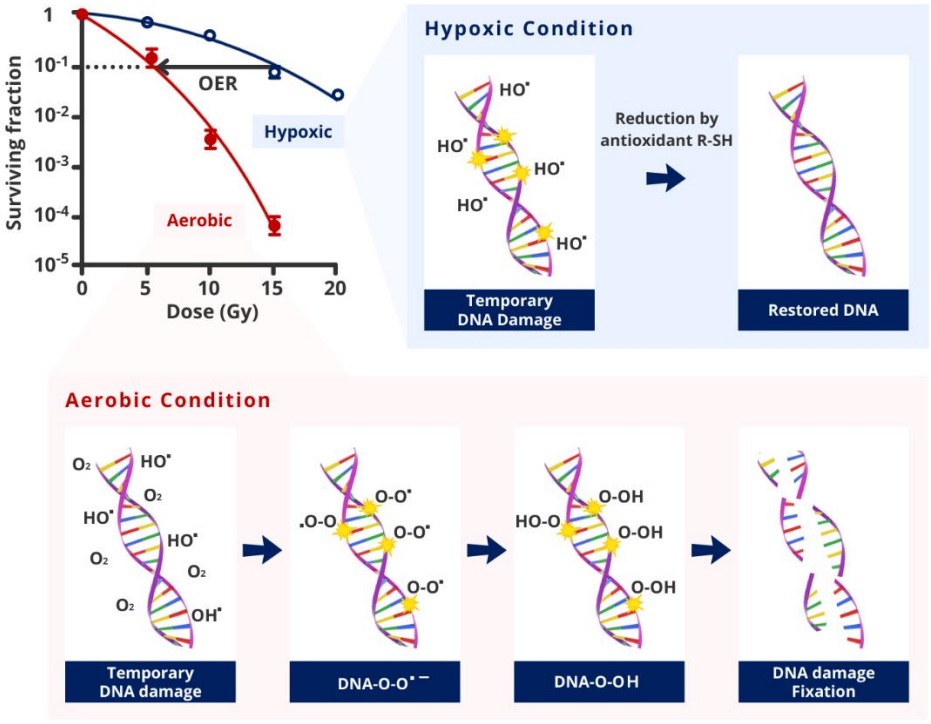
Fig. 3: Mode of action of KORTUC



When KORTUC is injected into a tumor, antioxidative enzymes, such as peroxidases and catalases, that are especially abundant in the radioresistant tumor begin to break H_2O down into water and oxygen accompanying an inactivation of these antioxidative enzymes. Then, the energy from the sudden radiation dose splits some of the remaining H_2O_2 into highly reactive hydroxyl radicals (OH•) which bind to and damage important parts of the tumor cells.

The newly released oxygen enhances this damage.

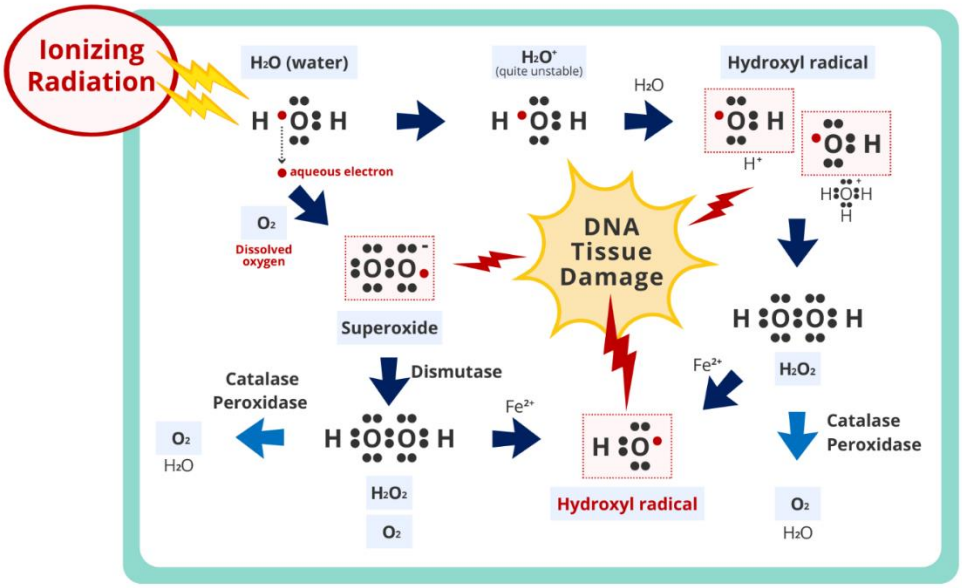
Fig. 4: The role of oxygen in fixing free radical (OH•) damage



When KORTUC is injected into a tumor, antioxidative enzymes, such as peroxidases and catalases, that are especially abundant in the tumor begin to break it down into water and oxygen. Then, the energy from the sudden radiation dose splits some of the remaining H2O2into highly reactive hydroxyl radicals (•OH) which bind to and damage important parts of the tumor cells.

The newly released oxygen enhances this damage. One mechanism is by causing sections of DNA to which •OH radicals are bound to suffer double-strand breaks. This usually makes the DNA unrepairable and results in cell death.

Fig. 5: Mechanisms how H_2O_2 and oxygen enhance radiation damage



Also, high levels of H_2O_2 neutralize the antioxidative enzymes, such as peroxidases and catalases, that protect tumor cells from the oxidative damage H_2O_2 can cause.