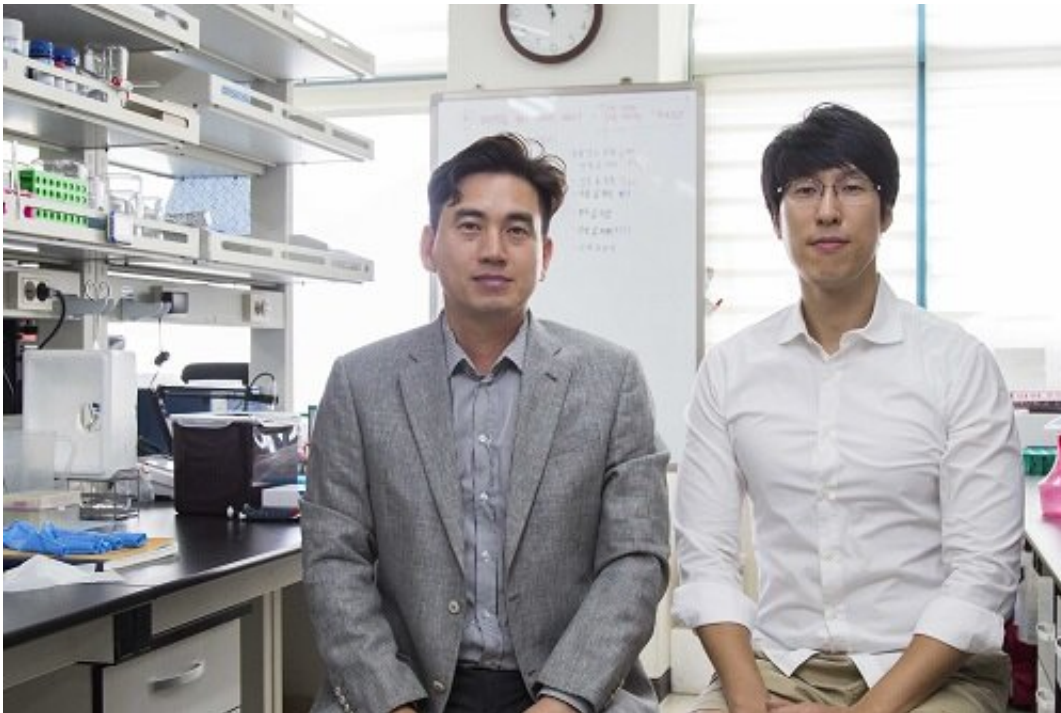


Researchers describe a mechanism inducing self-killing of cancer cells

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Professor Kim (left) and lead author Lee. Credit: The Korea Advanced Institute of Science and Technology (KAIST)

Researchers have described a new mechanism which induces the self-killing of cancer cells by perturbing ion homeostasis. A research team from the KAIST Department of Biochemical Engineering has developed helical polypeptide potassium ionophores that lead to the onset of programmed cell death. The ionophores increase the active oxygen

concentration to stress endoplasmic reticulum to the point of cellular death.

The electrochemical gradient between extracellular and intracellular conditions plays an important role in cell growth and metabolism. When a cell's ion homeostasis is disturbed, critical functions accelerating the activation of apoptosis are inhibited in the cell.

Although ionophores have been intensively used as an ion homeostasis disturber, the mechanisms of [cell death](#) have been unclear and the bio-applicability has been limited. In the study featured at *Advanced Science*, the team presented an alpha helical peptide-based anticancer agent that is capable of transporting [potassium ions](#) with water solubility. The cationic, hydrophilic, and [potassium](#) ionic groups were combined at the end of the peptide side chain to provide both ion transport and hydrophilic properties.

These peptide-based ionophores reduce the intracellular potassium concentration and at the same time increase the intracellular calcium concentration. Increased intracellular calcium concentrations produce intracellular reactive oxygen species, causing [endoplasmic reticulum](#) stress, and ultimately leading to apoptosis.

Anticancer effects were evaluated using tumor-bearing mice to confirm the [therapeutic effect](#), even in animal models. It was found that tumor growth was strongly inhibited by endoplasmic stress-mediated apoptosis.

Lead author Dr. Dae-Yong Lee said, "A peptide-based ionophore is more effective than conventional chemotherapeutic agents because it induces apoptosis via elevated reactive oxygen species levels. Professor Yeu-Chun Kim said he expects this new mechanism to be widely used as a new chemotherapeutic strategy. This research was funded by the National Research Foundation.

More information: DaeYong Lee et al. A Helical Polypeptide-Based Potassium Ionophore Induces Endoplasmic Reticulum Stress-Mediated Apoptosis by Perturbing Ion Homeostasis, *Advanced Science* (2019).

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