GIST develops nano anti-cancer technology that selectively starves cancer cells and attacks them with reactive oxygen species

- A joint research team led by Professors Inchan Kwon and Giyoong Tae of the Department of Materials Science and Engineering blocks the essential nutrient 'arginine' through an enzyme chain reaction activated only in cancer tissue, inducing reactive oxygen species-based cell death.

- Anticancer effects confirmed, including a maximum 4.6-fold increase in the accumulation of therapeutic enzymes within cancer tissue and an approximately 80% reduction in arginine; both efficacy and safety verified without side effects in animal experiments.

- Published in the international academic journal ***Biomaterials Research***

▲ (From left) Professor Inchan Kwon, Professor Giyoong Tae, Dr. Jae Hun Lee, and Junyoung Jung, a student in the integrated master's and doctoral program, Department of Materials Science and Engineering.

The Gwangju Institute of Science and Technology (GIST, President Kichul Lim) announced that a joint research team led by Professors Inchan Kwon and Giyoong Tae of the Department of Materials Science and Engineering has developed a "dual-enzyme-based anticancer system (RDC/DAO@NC)" that operates selectively only in cancer tissue.

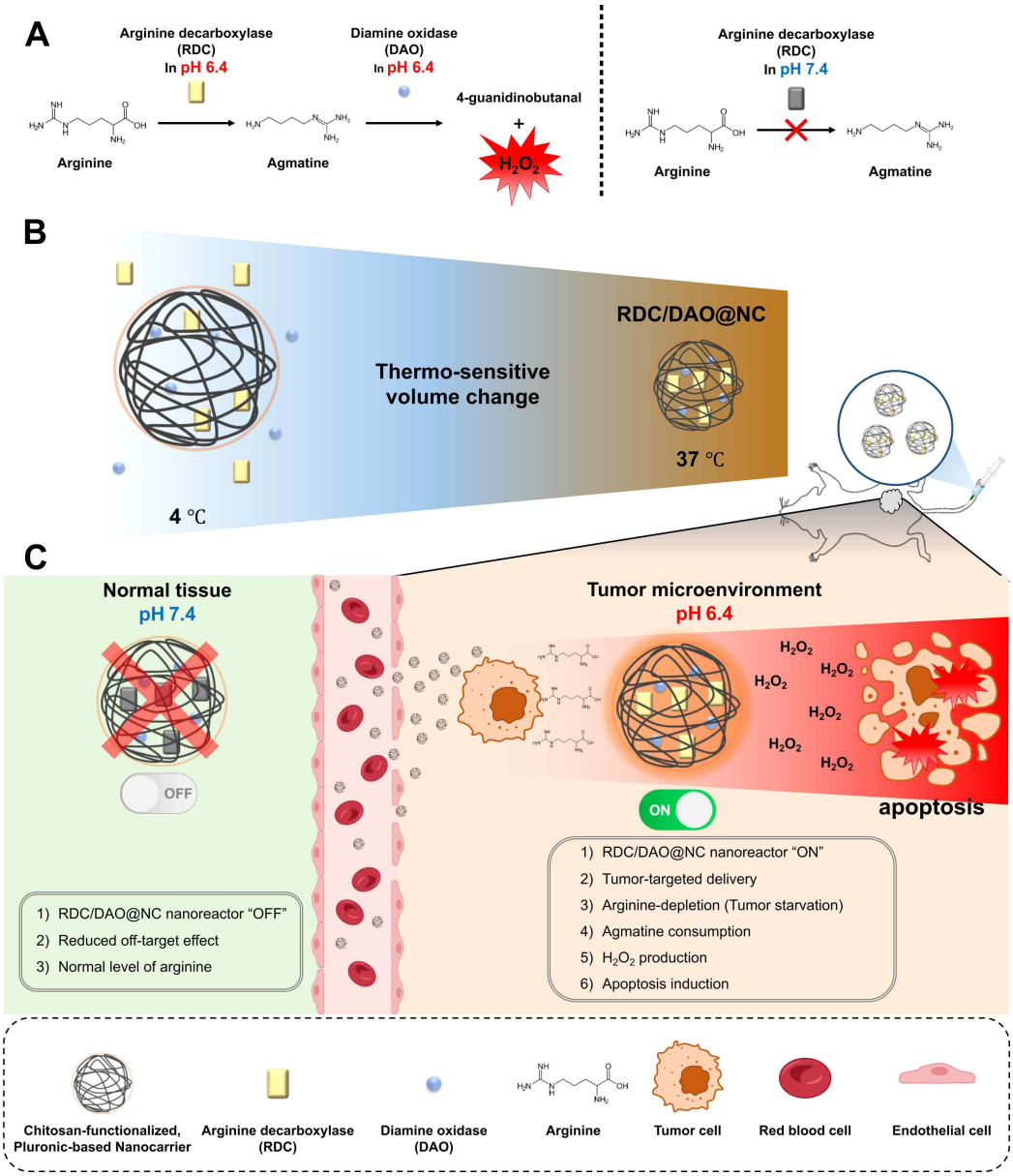
This technology works by starving cancer cells by removing arginine, an essential nutrient for cancer cells, while simultaneously generating reactive oxygen species to induce cell death. In particular, it is attracting attention as a next-generation precision anticancer strategy capable of minimizing damage to normal tissues, as the enzyme is designed to be activated only in the acidic environment of a tumor.

The research team implemented a cascade reaction by loading arginine decarboxylase (RDC), an enzyme that degrades arginine necessary for cancer cell growth, and diamine oxidase (DAO), which induces the generation of reactive oxygen species, onto a single nanocarrier (NC).

** arginine decarboxylase (RDC): An enzyme that converts arginine into agmatine. Although its activity is normally low, it possesses acidity-responsive characteristics in which it spontaneously transforms into an active structure in an acidic environment, thereby enhancing its function.*

** diamine oxidase (DAO): An enzyme that oxidatively degrades various diamine-based molecules, including agmatine. This process generates hydrogen peroxide (H_2O_2), and the resulting reactive oxygen species can induce localized oxidative stress. In addition, DAO plays a role in regulating diamine concentrations within the body and is known as an enzyme that mediates biochemical reactions within the tissue microenvironment.*

** nanocarrier (NC): A delivery vehicle that packages drugs or enzymes at a nanoscale to enhance in vivo stability and accumulation/retention within tumors. In this study, RDC and DAO were loaded together using a pluronic polymer-based nanocarrier combined with chitosan.*

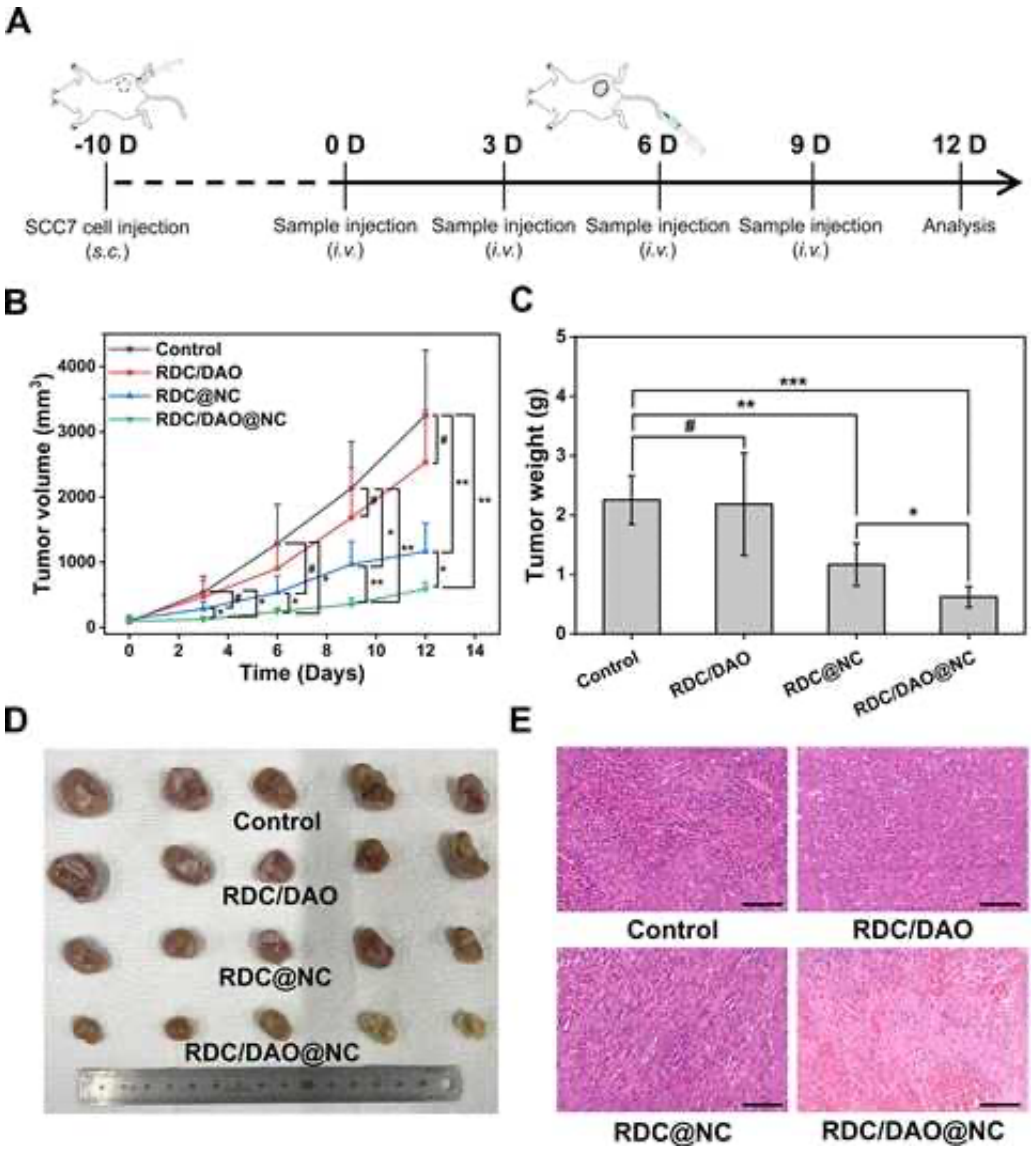


▲ ***Operating principle of the RDC/DAO@NC anticancer treatment system. This is a schematic diagram illustrating an enzymatic cascade reaction in which RDC is activated in an acidic tumor environment to decompose arginine into agmatine, which is then converted into hydrogen peroxide by DAO. While RDC activity remains low at normal pH, it becomes activated in the weakly acidic environment of a tumor, inducing arginine depletion and reactive oxygen species-based apoptosis.***

In anticancer treatment, it is crucial to effectively eliminate cancer cells while minimizing damage to normal tissues. However, existing targeted anticancer therapies have focused on designing drugs to deliver them to the tumor or release them within the tumor environment, which has led to limitations in that the actual therapeutic agent itself can also act within normal tissues.

The recently garnering attention "anticancer treatment inducing arginine depletion" can block the nutrient supply to cancer cells, but it also carries the potential to affect the metabolism and immune functions of normal cells.

To overcome these limitations, the research team developed a dual-enzyme-based anticancer system (RDC/DAO@NC) that 'starves and attacks' cancer cells.



▲ ***The anticancer efficacy of RDC/DAO@NC verified in animal experiments. When the sample was intravenously injected into SCC7 tumor model mice a total of four times at three-day intervals and tumor growth was compared, the RDC/DAO@NC administration group showed the greatest reduction in tumor size and weight. H&E staining results also confirmed that the tumor tissue structure in the RDC/DAO@NC administration group was significantly weakened.***

This treatment technology operates via a "chain reaction" in which two enzymes operate sequentially. First, the RDC enzyme removes arginine, a nutrient essential for cancer cell growth, thereby blocking the energy supply to the cancer cells.

Next, the DAO enzyme further decomposes agmatine, a byproduct generated during the RDC reaction, to produce hydrogen peroxide (H2O2). The reactive oxygen species produced at this stage induce strong oxidative stress in cancer cells, eventually leading to apoptosis.

In particular, the RDC enzyme is designed to be barely activated in normal environments and to operate selectively only in the weakly acidic environment of tumors, thereby minimizing its impact on normal tissues.

The research team loaded the two enzymes together into a single nanocarrier to reduce the reaction distance, thereby enabling a chain reaction to occur efficiently, much like a ‘nano-sized reaction space (nanoreactor).’

The research team verified the anticancer efficacy and safety of RDC/DAO@NC through cell and animal experiments.

In the cell experiments, the study compared a group treated with RDC alone, a group treated with both RDC and DAO simultaneously, and a group treated with RDC/DAO@NC, which carried both enzymes on a nanocarrier. The results showed that while the group treated with RDC alone exhibited an inhibitory effect on cancer cell proliferation, cell death was limited; however, when RDC and DAO were used together, the cell death effect was partially enhanced due to increased production of reactive oxygen species.

However, the nanocarrier-loaded group demonstrated the most powerful effect, with the cascading reaction speed increasing by up to 5.1 times. This result is attributed to the structure of the ‘nanoreactor,’ which is designed to allow the two enzymes to operate continuously over a short distance.

In the subsequent animal experiments, RDC/DAO@NC was intravenously administered to experimental mice a total of four times at three-day intervals. Consequently, the accumulation of enzymes within the tumor increased by up to 3.3 to 4.6 times, and the concentration of arginine within the tumor decreased by approximately 80%.

In addition, an anticancer effect was confirmed, resulting in a significant reduction in tumor size and weight, while an increase in reactive oxygen species (ROS) and elevated levels of apoptosis indicators were observed. Conversely, no weight loss or major organ toxicity was observed, verifying both therapeutic efficacy and safety.

This study is significant in that it goes beyond simply delivering drugs to tumors; it is designed so that the therapeutic enzyme itself is selectively activated only within the tumor microenvironment.

Furthermore, by simultaneously implementing metabolic therapy that blocks nutrient supply to cancer cells and ROS-based apoptosis, the study presents a new precision anticancer strategy that complements the limitations of existing arginine-depleting anticancer therapies.

The research team anticipates that by expanding the scope of application to various cancer types and verifying long-term safety, this technology can be developed into a next-generation enzyme-based anticancer platform through combination therapy with existing anticancer drugs and immunotherapies.

Professor Inchan Kwon said, "This study is a new anticancer strategy that combines a 'switch-type enzyme' that is activated only in the acidic environment of a tumor with a chain reaction between the two enzymes." He also added, "It is expected to complement the limitations of existing arginine-depleting anticancer treatments by simultaneously inducing metabolic treatment that starves cancer cells and reactive oxygen species-based cell death."

Professor Giyoong Tae stated, “While existing targeted anticancer therapies focused on delivering drugs to tumors, this study is distinct in that it limited the environment in which the therapeutic enzyme operates to the tumor itself,” adding, “It could also be expanded into combination strategies with other enzyme-based therapies or immuno-oncology in the future.”

This research, jointly supervised by Professors Inchan Kwon and Giyoong Tae of the Department of Materials Science and Engineering and conducted with integrated master’s and doctoral student Junyoung Jung and Dr. Jae Hun Lee as co-first authors, was supported by the Ministry of Science and ICT and the National Research Foundation of Korea’s Mid-Career Researcher Support Program.

The research results — A Tumor-Responsive Enzymatic Cascade System Inducing pH-Activable Metabolic Starvation and H_2O_2-Induced Apoptosis — were published online on May 15, 2026, in *Biomaterials Research*, a prominent international journal in the field

of biomaterials.

Meanwhile, GIST announced that this research achievement was considered to have both academic significance and potential for industrial application, and that discussions regarding technology transfer can be conducted through the Technology Commercialization Center (hgmoon@gist.ac.kr).