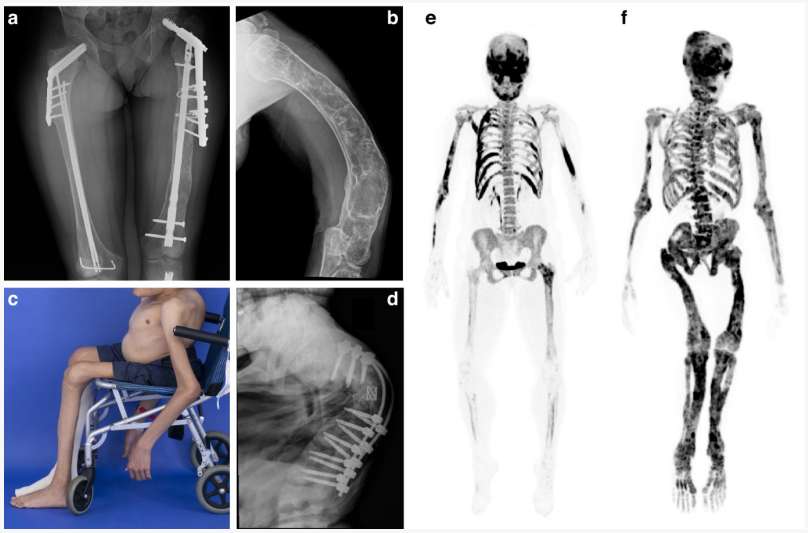
# RNA Editing Enzyme Reprograms Aggressive Bone Cancer Cells

*Researchers show that restoring adenosine deaminase acting on RNA 2 activity forces osteosarcoma cells to differentiate and become less aggressive*



Researchers show that editing activity of ADAR2 abolishes its proliferative effect on osteosarcoma cells and triggers terminal differentiation, indicating that ADAR2 acts as a tumor suppressor in osteosarcoma and may represent a novel therapeutic target.

CHINA, May 20, 2026 /EINPresswire.com/ -- Osteosarcoma is an aggressive bone cancer characterized by high rate of recurrence and metastasis. In a new study, researchers show that restoring the RNA-editing enzyme adenosine deaminase acting on RNA 2 (ADAR2) slows tumor growth, reduces invasion, promotes bone-like differentiation, and improves chemotherapy sensitivity in cell and mouse models. The findings identify IGFBP7 RNA editing as a key mechanism underlying these effects, highlighting a potential differentiation-based treatment strategy for pediatric patients with bone cancer.

Osteosarcoma is the most common primary bone cancer in children, adolescents, and young adults. Although chemotherapy and surgery have improved survival for localized disease, outcomes remain poor when tumors spread to the lungs or return after treatment. A major challenge is that osteosarcoma cells often remain locked in an immature developmental state, allowing them to grow rapidly and invade surrounding tissues. Thus, it is necessary to identify and develop new therapeutic targets and strategies.

To address this challenge, a research team led by Dr. Andrea Del Fattore, Head of the Bone Physiopathology Research Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy and Prof. Angela Gallo from the Unit of Genetic and Epigenetics of pediatric tumors, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy investigated whether the RNA-editing enzyme adenosine deaminase acting on RNA 2 (ADAR2) could reverse the aggressive behavior of osteosarcoma

cells. Using patient datasets, laboratory cell models, transcriptomic analysis, and mouse studies, the researchers examined how restoring ADAR2 affects tumor growth and bone differentiation. Their findings were published in Volume 14 of the journal Bone Research on April 03, 2026.

The team first found that ADAR2 levels naturally rise when healthy mesenchymal stem cells develop into bone-forming osteoblasts. “In contrast, osteosarcoma tissues and highly aggressive cancer cell lines showed markedly reduced ADAR2 expression. Lower ADAR2 levels were also associated with poorer metastasis-free survival and overall survival in patient datasets, suggesting that loss of this enzyme may be linked to more dangerous disease” says Dr. Michela Rossi from the Bone Physiopathology Research Unit, Bambino Gesù Children’s Hospital, first author of the manuscript.

When the researchers increased ADAR2 expression in osteosarcoma cells, tumor-like behavior declined sharply, cell growth slowed, invasive capacity dropped, and migration was reduced. In one osteosarcoma model, the treated cells began producing mineralized matrix, a hallmark of mature bone tissue. Genes linked to osteoblast differentiation increased, while markers associated with stemness and malignancy declined.

“Our findings suggest that osteosarcoma cells are not irreversibly fixed in an aggressive state. By restoring ADAR2, we were able to reactivate developmental programs that steer these cells toward a more mature and less harmful identity,” says Dr.Del Fattore.

The benefits extended beyond cell culture. In mice implanted with human osteosarcoma cells, ADAR2-restored tumors were smaller, less invasive, and less likely to spread to the lungs or liver. Some animals developed minimal tumor burden compared with controls. The treated cells also showed greater sensitivity to methotrexate and selected anti-cancer compounds, indicating that ADAR2-based approaches may strengthen existing therapies rather than replace them.

To understand how ADAR2 exerts these effects, the team analyzed RNA changes across treated cells. They identified insulin-like growth factor binding protein 7 (IGFBP7) as one of the most strongly edited RNA targets. Normally, IGFBP7 can stimulate growth-related IGF signaling pathways that help cancer cells survive and proliferate. However, once edited by ADAR2, this signal was weakened. The edited form no longer promoted proliferation and instead supported expression of bone-development regulators such as runt-related transcription factor 2.

“In my lab, we have studied RNA editing for years, focusing on the role of epitranscriptomic reprogramming in highly aggressive brain tumors. Building on this work and in collaboration with Dr. Del Fattore’s team, we have now demonstrated that ADAR2 also plays a similar tumor-suppressive role in osteosarcoma, opening the way to novel therapeutic targets for this and other tumours. ” says Prof. Gallo.

The findings may have broader ripple effects beyond bone cancer. RNA editing is increasingly implicated in leukemia, brain tumors, and several solid cancers, meaning the study could

stimulate collaborations among pediatric oncologists, RNA biologists, and drug developers. Over the next decade, therapies designed to reprogram cancer cells toward maturation could reduce reliance on highly toxic treatment regimens.

Overall, the study provides strong preclinical evidence that restoring ADAR2 can suppress osteosarcoma progression by promoting terminal bone differentiation and weakening metastatic behavior. By targeting the developmental state of cancer cells rather than only destroying them, the research points toward a promising new direction for future pediatric cancer therapy.

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Reference
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About Bambino Gesù Children's Hospital, Italy
Bambino Gesù Children's Hospital, Rome, Italy, is one of Europe's leading pediatric research and healthcare institutions, dedicated exclusively to children's medicine. It serves as a major referral center for complex and rare childhood diseases, integrating advanced clinical care with translational research. The hospital is recognized as an IRCCS scientific institute and is known for expertise in oncology, genetics, rare diseases, surgery, and regenerative medicine. Its multidisciplinary teams collaborate internationally to develop innovative diagnostics and therapies that improve child health outcomes.
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About Dr. Andrea Del Fattore
Dr. Andrea Del Fattore is the Head of the Bone Physiopathology Research Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy. His research focuses on bone biology, osteoclasts, osteoblasts, bone metabolism, osteogenic differentiation, bone histology, regenerative medicine, skeletal disorders, and translational medicine. He has authored 94 publications with 5,858 citations, reflecting major influence in musculoskeletal research.

About Prof. Angela Gallo
Prof. Angela Gallo is affiliated with the Unit of Genetic and Epigenetics of paediatric tumours, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy. Her scientific work focuses on RNA biology, particularly A-to-I RNA editing, epitranscriptomics, ADAR enzymes, non-coding RNA, microRNA, and cancer mechanisms. She has authored 60 publications with 3,544 citations and has received multiple grants on RNA editing and cancer. She is a founder and active member of the international "The Human RNome Project", reflecting the strong impact of her research team at the international level.

About Dr. Michela Rossi
Dr. Michela Rossi is affiliated to Bone Physiopathology Research Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, headed by Dr. Del Fattore. Her scientific activity focuses on rare bone diseases, especially Osteosarcoma and osteolytic diseases. She has authored 27 publications with 810 citations.

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