# Raphael Rodriguez’s Fentomycin-1 offers new hope by targeting iron metabolism to halt cancer metastasis



When Raphael Rodriguez realised that medical school was not his calling, he redefined his ambitions, pivoting from the clinic to the lab. "I knew I was still destined to help people somehow," he reflected, highlighting his determination to contribute meaningfully to public health. This shift led him to collaborate with esteemed organic chemists at Oxford and Cambridge, where he discovered the profound potential of chemical biology in treating diseases, particularly cancer.

Years of rigorous research culminated in the development of Fentomycin-1, a promising new compound that has the potential to dramatically alter the landscape of cancer treatment. This innovative molecule targets a critical aspect of cancer's lethality – its ability to metastasise, a process responsible for at least 70 percent of cancer-related deaths. Rodriguez observed, "When you look at literature, you realise that 70 percent of cancer patients do not succumb to the primary tumour, but the metastatic spread." This staggering statistic underscores the urgency for therapies that can effectively address metastasis.

Fentomycin-1 exploits a biochemical quirk of cancer cells – their voracious appetite for iron. Cancer cells accumulate this metal within lysosomes, allowing for aggressive growth and, paradoxically, creating a vulnerability. The compound activates ferroptosis, a mechanism that triggers death from within by targeting the iron-rich environment of these cells. In early laboratory tests, Rodriguez's team found that metastatic cells could be annihilated in under 12 hours, a result that was met with excitement. Rodríguez articulated the impact of this discovery, stating, “It was very gratifying for us to see that we are capable of designing a compound that does what we wanted to do.”

The application of Fentomycin-1 has been tested across various aggressive cancers, including pancreatic cancer, breast cancer, and sarcomas, which are known for their high drug resistance and poor survival rates. In animal models, the drug not only curtailed tumour growth but also spurred immune responses, suggesting it may be advantageous when used alongside existing therapies like chemotherapy. By targeting the heightened iron levels typical in cancer cells, Fentomycin-1 minimises harm to surrounding healthy tissue, a crucial advantage in oncological treatments.

Clinical trials remain essential to validate the effectiveness of Fentomycin-1 in humans. Rodriguez emphasised the need for substantial funding and rigorous testing to explore how the compound interacts within the human body, stating, "At this point in time, we are happy with the compound we made," signalling a cautious optimism about the future of his research.

Despite the success observed in animal studies, the path to clinical application is fraught with complexity. Metastatic cancer cells exhibit remarkable adaptability, often evading chemotherapy by becoming resistant to drugs or repairing DNA damage inflicted by radiation treatments. The National Cancer Institute estimated in 2018 that over 623,000 Americans were living with the six most common types of metastatic cancers, a number projected to climb to nearly 700,000 by 2025. This grim statistic highlights the critical need for innovative therapies like Fentomycin-1 to combat the challenge posed by metastatic disease.

Rodriguez’s research has opened up new avenues in targeted cancer therapies, focusing on the specific iron metabolism disruptions that characterise aggressive tumour types. His findings contribute to the growing body of literature that suggests dysregulation of iron within the tumour microenvironment plays a key role in cancer progression. As the scientific community begins to understand the implications of targeting iron metabolism, compounds like Fentomycin-1 could represent a significant step forward in the quest to save lives disrupted by cancer.

Yet for Rodriguez, the journey is only beginning. He and his team continue to navigate the challenges of bringing their discoveries from the lab bench to the clinic, determined to realise their vision of a more effective, targeted approach to cancer treatment.

### Reference Map

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## Bibliography

1. <https://www.dailymail.co.uk/health/article-14740251/medical-school-dropout-end-cancer-deaths-iron.html?ns_mchannel=rss&ns_campaign=1490&ito=1490> - Please view link - unable to able to access data
2. <https://pubmed.ncbi.nlm.nih.gov/38659936/> - This preprint article discusses the development of fentomycin, a bifunctional compound designed to induce ferroptosis in cancer cells by activating lysosomal iron. The study demonstrates that fentomycin effectively kills primary sarcoma and pancreatic ductal adenocarcinoma cells, preferentially targeting iron-rich CD44^high cell subpopulations associated with metastatic disease and drug resistance. In vivo experiments in a murine model of breast cancer metastasis show that fentomycin depletes CD44^high cells and reduces intranodal tumor growth, highlighting the potential of targeting lysosomal iron redox chemistry for therapeutic benefits in cancer treatment.
3. <https://institut-curie.org/news/new-class-molecules-against-cancer-cells-refractory-standard-treatments> - Institut Curie reports on the development of fentomycin (Fento-1), a fluorescent molecule designed to induce ferroptosis in cancer cells by targeting lysosomal iron. Pre-clinical studies demonstrate significant reduction in tumor growth in models of metastatic breast cancer and pronounced cytotoxic effects on biopsies from pancreatic cancer and sarcoma patients. The research suggests that fentomycin could serve as a therapeutic avenue complementing current chemotherapy, particularly for cancers that are pro-metastatic and refractory to standard treatments. The study emphasizes the need for clinical tests to validate these findings.
4. <https://austinpublishinggroup.com/hematology/fulltext/hematology-v8-id1351.php> - This article explores the role of iron metabolism in cancer, highlighting how dysregulation, particularly the accumulation of iron within cells, contributes to tumorigenesis, progression, metastasis, and alterations in the tumor microenvironment. It discusses the increased dependency of cancer cells on iron for growth and proliferation compared to healthy cells, and how proteins involved in iron regulation, such as TFR-1, are overexpressed in various cancers, leading to elevated intracellular iron concentrations and reactive oxygen species production, which promote tumor growth and metastasis.
5. <https://www.spandidos-publications.com/10.3892/ijo.2019.4720> - This review examines the complex processes of iron-sulfur cluster biogenesis and mitochondrial iron transport, emphasizing their roles in cellular functions like the mitochondrial respiratory chain, DNA replication, and RNA modification. It highlights how high concentrations of iron and these enzymes significantly promote cellular growth in tumors. The review also discusses the importance of iron-sulfur clusters in mitochondrial function and their potential as targets for cancer therapy, noting that inhibitors of these clusters have been identified as potential anticancer agents.
6. <https://aacrjournals.org/cancerres/article-abstract/81/9/2289/670615/Targeting-Mitochondrial-Iron-Metabolism-Suppresses> - This study investigates the use of mitochondrially targeted deferoxamine (mitoDFO) as a novel approach to preferentially target cancer cells. The research demonstrates that mitoDFO impairs mitochondrial respiration, disrupts iron-sulfur cluster and heme biogenesis, and induces mitochondrial dysfunction and mitophagy in cancer cells. In vitro and in vivo experiments show that mitoDFO suppresses tumor growth and metastasis, highlighting the importance of mitochondrial iron metabolism in cancer cells and suggesting that targeting this pathway could be an effective anticancer strategy.
7. <https://pubmed.ncbi.nlm.nih.gov/36890422/> - This study examines the role of DMT1 inhibition and salinomycin in promoting ferroptosis by targeting lysosomal iron in head and neck cancer (HNC) cells. The research shows that silencing DMT1 or treating with salinomycin increases the labile iron pool, intracellular ferrous and total iron contents, and lipid peroxidation, leading to enhanced cell death. These findings suggest that DMT1 inhibition or salinomycin treatment can promote ferroptosis in HNC cells, offering a novel strategy for targeting iron-avid cancer cells.