CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120408

Project Title:
Anti-Cancer Drugs to Treat Cancer Pain

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

One of the most dreaded complications of cancer is severe, unrelenting pain. Opiate narcotics, which have been used for centuries, are still the primary treatment for severe cancer pain. Unfortunately, narcotics are not very effective against pain caused by nerve injury, invasion or compression, which is a prominent component of cancer pain. Opiates also become less effective over time because tolerance develops to their pain-relieving effects. For years, narcotic tolerance and cancer pain have long been thought to utilize similar cellular signals. However, these mechanisms are poorly understood. We recently reformulated Gleevec, a commonly used anti-cancer drug that blocks the platelet-derived growth factor receptor (PDGFR), so it would cross the blood-brain barrier. We made the amazing discoveries that Gleevec eliminates morphine tolerance and that nerve injury pain can be completely reversed by combining morphine and Gleevec. Our findings represent a major conceptual breakthrough in understanding the complex relationships between pain, pain relief, and narcotic tolerance. We found that PDGFR signaling in animals selectively causes tolerance without directly altering the pain-relieving effects of morphine. The data also suggest that PDGFR signaling caused by nerve injury pain renders opiates ineffective. Taken together, our findings suggest the groundbreaking hypothesis that the PDGFR may be a “common integrator” of the myriad signals that underlie cancer pain and tolerance. This could represent a major breakthrough in our understanding and treatment of cancer pain. Untold numbers of cancer patients suffer in agony, either because opiates are ineffective or tolerance develops. The fact that several widely used anti-cancer drugs target the PDGFR provides added incentive for pursuing these important studies, as positive results could be readily translated into meaningful reductions in the pain and suffering of cancer patients during the lifetime of the CPRIT.