**Iron and cancer:**

**An unsuspecting relationship brings insight to the future of cancer research.**

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Cancer is the second leading cause of death worldwide, and despite major advancements in our knowledge of how it arises, the prognosis of this illness remains grim. Before the turn of the century, progress in the field of cancer treatment proceeded sluggishly. In recent years, however, the rate of progress has increased dramatically due to new ideas brought about by brilliant scientists. One such group of researchers are those in the Laboratory of Mckale Montgomery, an assistant professor at Oklahoma State University. Last month, Dr. Montgomery and I were able to sit down and discuss recent progress brought about (M. Montgomery, personal communication, March 30 2021).

Dr. Montgomery describes her laboratory’s current focus as “understanding the mechanisms involved in iron metabolism in cancer cells”. Specifically, they are focused on understanding how certain mutations can alter the nature of iron metabolism in these cells. This present goal of research hopes to build on two papers that the Montgomery lab recently published. In their 2019 publication titled *Distinct TP53 Mutation Subtypes Differentially Influence Cellular Iron Metabolism*, they describe how mutations of the TP53 gene can disrupt the normal processes of how iron is metabolized at a molecular level. What are the broader implications of this research, though? Montgomery explained, “Mutations of the TP53 gene are present in over half of all cancers. Under normal circumstances TP53 acts as a Tumor Suppressor gene that regulates how much iron is available for a cell.” Too much iron inside of a cell can promote tumorogenesis and cancer cell growth, she explained. In their most recent publication, the Montgomery lab found that a certain mutation of the TP53 gene can also alter the sensitivity of cells to induce an iron-dependent form of programmed cellular death called ferroptosis. What does all of this mean in terms of developing new treatments for cancer? The answer can ultimately be found in the fundamental technique of finding properties that are unique to cancer cells. By differentiating cancer cells from normal cells, novel therapies can be developed. Dr. Montgomery noted, evidence suggests that since TP53 is mutated in half of all cancers, then iron metabolism may very well be disrupted in half of all cancers as well. “Since iron metabolism is ‘messed up’ in half of all cancers, can we target these types of cells?” Montgomery proposed. She added that today’s evidence suggests that this may indeed be possible, but further investigations must continue to be certain.

What does this all mean for the future? Regulating dietary intake of iron is one potential strategy to prevent and supplement the treatment of cancer, Montgomery pointed out. She closed the interview by acknowledging approaches like this and explorations into exploiting ferroptosis will be at the forefront of research for many years to come. Nevertheless, the progress of cancer research is certainly reaching a compelling level with no indication of slowing down soon.

References

Clarke SL, Thompson LR, Dandekar E, Srinivasan A, Montgomery MR. Distinct TP53 Mutation Subtypes Differentially Influence Cellular Iron Metabolism. Nutrients. 2019 Sep 7;11(9):2144. doi: 10.3390/nu11092144. PMID: 31500291; PMCID: PMC6769808.

Thompson, L. R., Oliveira, T. G., Hermann, E. R., Chowanadisai, W., Clarke, S. L., & Montgomery, M. R. (2020). Distinct TP53 Mutation Types Exhibit Increased Sensitivity to Ferroptosis Independently of Changes in Iron Regulatory Protein Activity. *International journal of molecular sciences*, *21*(18), 6751. https://doi.org/10.3390/ijms21186751