Finding Effective Dosing for Copper Chemotherapy Mimics Can Copper Replace Platinum?

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Three platinum anticancer compounds have been used for over 40 years in the United States. Despite their longtime use, it wasn't until 2017 that it was discovered that one of the platinum drugs, oxaliplatin, caused a different cell death pathway than the other two compounds (cisplatin and carboplatin). This type of stress called nucleolar stress is a disruption of the ribosome biogenesis pathway (the pathway to create ribosomes). But platinum might not be the only metal to be able to induce this stress pathway, copper shares similar molecular shape as platinum, is less toxic, and much cheaper. Could copper replace platinum? We studied a copper mimic of oxaliplatin called CuDACH in yeast. Previously, it was found that our genetically modified yeast strain with the protein RRN3 marked with Neon Green fluorescent protein could be a marker for nucleolar stress. But researchers were having trouble finding effective dosing of yeast due to the cell wall. We found that effective dosing for yeast with CuDACH is between 20 and 30 mM. When treated with 25 mM treatment at 24 hours, our yeast showed the morphological changes where the protein moved. Our results match the positive control of hydrogen peroxide treatment. This shows that upon high treatment, our copper mimic induces stress in yeast and is causing oxidative stress which is a potential precursor to nucleolar stress. Further research will attempt to untangle oxidative and nucleolar stress with the copper compounds in yeast.

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