

Metal chemotherapy drugs boost the impact of immunotherapy in cancer

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Due to their powerful tumour-killing effect, metal-based chemotherapies are frequently used in cancer treatment. However, it was hitherto assumed that they damaged the immune system, because of their cytotoxic (cell-damaging) effect even against dividing healthy cells. In a scientific review produced by the Translational Cancer Therapy Research cluster, established by the University of Vienna and MedUni Vienna, it has now been demonstrated that the opposite is true: metal-based chemotherapies can even boost the immune response against cancer and hence strengthen immunotherapies, because they render the cancer cells visible and eliminate inhibitory components of the immune system, amongst other things. The article appeared in *Chemical Reviews*.

In its review, the inter-university Translational Cancer Therapy Research cluster examined all the papers (more than 1,300 [scientific articles](#) in total) relating to the interaction between the immune system and metal chemotherapy drugs. As well as looking at publications from the last 30 years or so, lead author Walter Berger from MedUni Vienna and his colleagues also discuss new aspects and provide a comprehensive overview.

Combination therapies are the future

Walter Berger, Deputy Head of MedUni Vienna's Institute of Cancer Research, member of the Comprehensive Cancer Center (CCC) of MedUni Vienna/Vienna General Hospital and one of the two directors of the interuniversity research cluster explains: "Even viewed from a global perspective, we are one of the few translational research clusters where experts in synthesis chemistry, basic researchers in cell and molecular

biology and clinical oncologists work directly together to develop new [cancer](#) treatments. And that is why we were invited to produce this review. The results clearly show that the combination of metal chemotherapy drugs and immunotherapies are among the most promising current and future treatment concepts."

Synergistic effects

The explanation behind this finding is this. Every cancer follows a long fight by the immune system against the potential cancer cells, which the immune system eventually loses. This happens because the tumour either manages to go undetected as something foreign or manages to control the immune cells and immobilise them. Metal chemotherapy drugs not only destroy tumour cells but preferentially also the "burnt out" or inhibitory components of the immune system. In response to this, the immune system renews itself from stem cells so that it is rejuvenated, as it were, and fully functional to resume the fight against cancer.

Metal-based chemotherapy therefore enhances the effect of immune checkpoint inhibitors. The reason for this is that [cancer cells](#) develop from the body's own cells. The immune system is trained to protect endogenous cells and therefore finds it difficult to detect tumour cells. Metal-based chemotherapies can now kill the tumour cells as they mutate during the process of disintegration. This "otherness" renders them once again visible to the immune system and therefore open to attack, a mechanism known as immunogenic cell death. In parallel, the tumour cells strive to combat the effect of the chemotherapy drug by increasing their mutation rate. However, each new mutation that is produced in this way can potentially be more easily recognised by the rejuvenated immune system. Hence the [immune system](#) seems to preferentially attack chemo-resistant tumour cell clones.

More information: Bernhard Engliger et al. Metal Drugs and the

Anticancer Immune Response, *Chemical Reviews* (2018). DOI: [10.1021/acs.chemrev.8b00396](https://doi.org/10.1021/acs.chemrev.8b00396)

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