Anti-Cancer Combination Therapy with Potential for Reduced Toxicity

INI-43, a small molecule inhibitor of nuclear transport protein Knβ1, in combination with Cisplatin, shows synergistic anti-cancer effects

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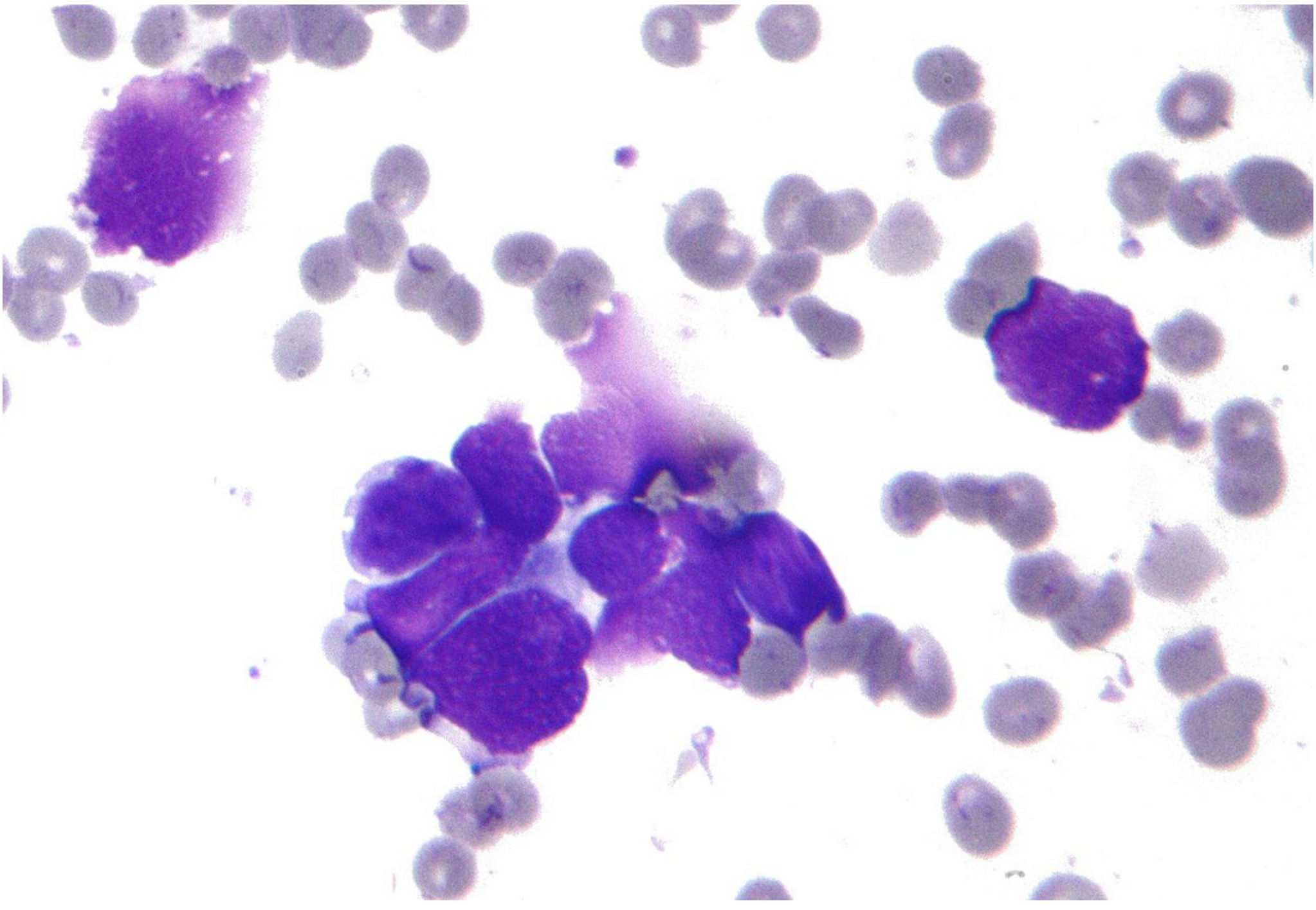

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Background

Various cancers, including gynecological cancers, are becoming resistant or insensitive to platinum-based chemotherapy and consequently higher dosages are required to be effective. Unfortunately, most of these chemotherapeutic drugs cause undesirable systemic effects such as cardiac or renal toxicity, alopecia, marrow aplasia, nausea, and vomiting. There is thus a critical need for new therapies or combination therapies with superior anti-cancer effects, yet with fewer side-effects and lower cancer resistance.

The inventors have previously demonstrated that specific small molecule inhibitors of the nuclear transport protein Karyopherin Beta (β) 1 have superior cell-killing effects to Platinum-based chemo at reduced toxicity (i.e., no toxicity on non-cancer cells, targeting only the cancer cells). Please see advertisement https://app.in-part.com/technologies/rOzNYkAe0MBQ for a detailed discussion of this anti-cancer therapy, for which UCT in conjuction with the University of Louisville have filed patents. The lead molecule is codenamed INI-43 or C43 (a quinoxaline-based derivative).

The inventors have further investigated the potential of INI-43 to be used in conjunction with other anti-cancer drugs as an anti-cancer combination therapy. A new technology flowing from this work is what is described in this advertisement, and has also been patented.

Technology Overview

The technology is an anti-cancer combination therapy consisting of an effective dose of a small molecule inhibitor of nuclear transport protein Karyopherin Beta (β) 1 as previously patented and a effective dose of any Platinum-based chemotherapy. *In vitro* data generated by UCT showed that the combination of INI-43 and Cisplatin leads to selective cell death at significantly higher rates than predicted in cervical and oesophageal cancer models. The combination shows clear synergism in that the combined cancer-killing effect is significantly higher than what can be expected if one considers the known cell-killing abilities of each drug separately. This combination therapy thus holds great promise for providing effective chemo at reduced toxicity and with lower side effects. The next stage of the development includes *in vivo* activity and ADMET tests, dosage determination, clinical trials and regulatory approvals.

Benefits

The main benefit is that the combination therapy potentially allows for patients to be treated with lower dosages of Cisplatin or other Platin-based chemo, reducing the overall toxicity, but maintaining the same or superior anti-cancer effect due to the synergistic effect between Cisplatin and INI-43. INI-43 on its own has been shown to have lower toxicity than Cisplatin (no toxicity on non-cancer cells). Cisplatin on the other hand does not differentiate between cancer and non-cancer cells, which results in adverse side effects and long-term complications.

Applications

In applications where advanced-stage cancer requires very high dosages of Cisplatin to be effective, the new combination therapy could potentially be used to alleviate side effects by reducing Cisplatin dose.

Opportunity

UCT is looking for development partners to assist with pre-clinical and clinical trials as well as regulatory requirements and potentially a licensing partner for the commercialisation of the combination therapy. A commercialisation strategy has not yet been formulated.

Patents

- PCT patent application number PCT/IB2021/057054

IP Status

- Patent application submitted

Seeking

- Development partner
- Licensing