Max-Planck-Innovation

Technology Offer

Novel biomarkers and therapeutic indications for PARP1 inhibitors

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HR-defective cancers are a class of malignancies characterized by impaired DNA repair mechanisms, typically resulting from mutations or deficiencies in genes involved in the Homologous Recombination (HR) pathway, such as BRCA1 and BRCA2. These cancers pose significant challenges in treatment due to their inherent resistance to standard therapies.

Poly ADP-ribose Polymerase 1 (PARP1) inhibitors represent a promising targeted therapy class designed to exploit the vulnerabilities of HR-defective cancers. By inhibiting PARP1 in HR-defective cancer cells, synthetic lethality is created as these cells are further compromised in their DNA repair capabilities. PARP1 inhibitors, such as olaparib, have shown remarkable clinical efficacy in treating HR-defective cancers, notably those associated with BRCA1 and BRCA2 mutations. These inhibitors have gained regulatory approval for the treatment of some malignancies, including ovarian and breast cancer.

However, only a small fraction of patients and a limited number of cancer types fall under the HR-defective category and can therefore be treated with PARP1 inhibitors.

Technology

Researchers at the Max Planck Institute for Biology of Ageing have identified **UBQLN1 and UBQLN4 as novel promising targets** that repress the **HR repair pathway**. These targets are frequently overexpressed in multiple cancers and are associated with poor survival rates. Importantly, their overexpression is not exclusive to known HR-deficient tumors but extends to a **broader spectrum of cancers**, including **lung adenocarcinoma** and others previously unconnected to HR deficiency.

Recent preclinical studies have demonstrated the potential of **using PARP1 inhibitors in cancers overexpressing these novel targets.** Notably, in *autochthonous animal models*, treatment with PARP1 inhibitors resulted in a significant survival benefit in animals overexpressing these targets compared to wild type animals.

Therefore, this discovery allows to **extend the number of cancer indications** and patients that will respond to a therapy with PARP1 inhibitors.

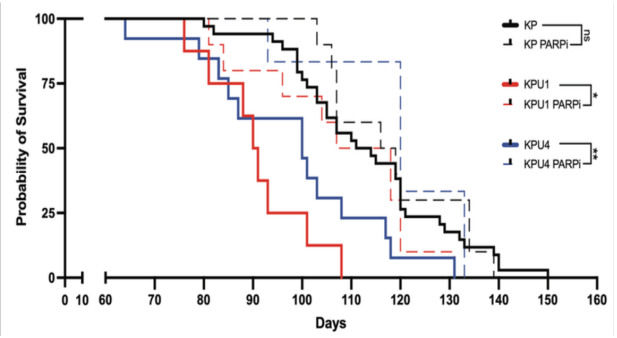

Fig. 1: Kaplan-Meier curves depicting the overall survival of *Kras*$^{LSL.G12D/wt;Tp53fl/fl}$ (KP), KP+*Rosa26*$^{LSL.Ubqln4/wt}$ (KPU4) and KP+*Rosa26*$^{LSL.Ubqln1/wt}$ (KPU1) mice after intratracheal induction with Adeno-Cre virus. Solid lines indicate untreated animals. Dashed lines indicate treated animals with PARP1 inhibitor.

Patent Information

Priority Patent Application has been filed in September 2023.

Opportunity

We are open to **research collaborations** or **license agreements** to accelerate the integration of this promising discovery into the clinical practice.

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