

New Ultra-Long Circulating Nanoparticle Developed for Chronic Myeloid Leukemia

2020-09-05 By conjugating CHMFL-ABL-053 to an amphiphilic polymer and subsequent self-assembling into a nanoparticle (NP) with a high loading, an ultra-long circulating nanomaterial was prepared by researchers recently.

Developed by Drs. FU Liyi and ZOU Fengming led by Profs. LIU Qingsong and LIU Jing from the Institute of Health & Medical Technology, <u>Hefei Institutes of Physical Science</u>, the formulation could greatly improve its solubility and drastically extended its circulation halflife.

Chronic myeloid leukemia (CML) is a clonal hematopoietic stem cell myeloproliferative disease, which is primarily caused by the chromosomal translocation between the Abelson (ABL) gene and the breakpoint cluster region (BCR) gene. Although the FDA-approved BCR-ABL inhibitors, such as Imatinib and Dasatinib etc. could greatly improve the 10-year survival rate of the patients, their off-targets, such as DDR1/2 and c-kit, may lead to the decrease of mast cells, vascular adverse events and other undesired side effects.

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(A) Self-assembly of the NPs and (B) their targeting of CML on two models.

Previously related research was conducted by Prof. Liu Qingsong and Prof. Liu Jing's group. And the BCR-ABL inhibitor CHMFL-ABL-053 had a better selectivity to the target of BCR-ABL over other protein kinases. However, like all of this class of inhibitors, it must be treated orally every day due to its short half-life, which would not only increase the economic burden of patients, but also lead to cumulative toxicities. This time, the team pushed <u>their work</u> further to make a modification based on their previous work. In the 150 days' long-term engraftment model experiment, long intravenous dosing intervals of the NPs (every 4 or 8 days) exhibited much better survival and negligible toxicities as compared to daily oral administration of the inhibitor.

The NPs showed excellent inhibition of tumor growth in the subcutaneous xenograft model. The excellent anti-leukemic efficacy of the NPs in the long injection cycle on both models might provide a novel, effective and safe therapeutic strategy for BCR-ABL-positive CML.

Read the original article on Chinese Academy of Sciences (CAS).