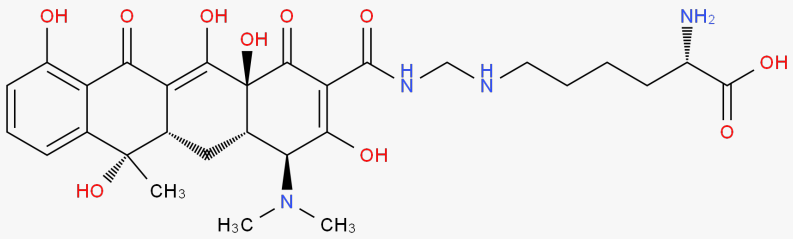
Lymecycline reverses acquired drug resistance in non–small-cell lung cancer

A study finds Lymecycline reverses acquired EGFR-TKI resistance in non–small-cell lung cancer by targeting GRB2.



Lymecycline

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PASADENA, CALIFORNIA, UNITED STATES, November 2, 2020 /EINPresswire.com/ -- In a recent study, researchers from China discovered lymecycline has the ability to reverse acquired EGFR-TKI resistance in cell lines and animal models, suggesting a potential therapeutic agent for acquired EGFR-TKI resistant non-small-cell cancer (NSCLC) and improve the prognosis of patients.

NSCLC is any type of epithelial lung cancer other than small cell lung carcinoma (SCLC), which accounts for about 85% of all lung cancers. Epidermal growth factor receptor (EGFR) mutations are found in 10–35 % of NSCLCs and first- and second-generation epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) were first-line treatments (e.g. Icotinib) for patients with this mutation. However, about 30 % of responders relapsed within six months because of acquired resistance. Acquired EGFR-TKI resistance limits the therapeutic benefit of TKIs. To discover drugs that reverse this effect, researchers from the First Hospital of China Medical University used Connectivity Map (CMap) to performs computational drug repositioning using a reference database based on genes and pathways related to NSCLC and its treatments. They discovered that regulated gene expression and reversed acquired EGFR-TKI resistance but has not been previously studied in cancer treatment. To confirm the findings of the network pharmacology studies, two Icotinib resistant cell lines were constructed and lymecycline's ability to suppress the proliferation of Icotinib resistant cells in vitro and in vivo was then evaluated.

Here is what they found: combined Lymecycline and Icotinib treatment produced a synergistic effect and induced apoptosis. Cell proliferation in resistant cancer cells was significantly inhibited by the combined Lymecycline and Icotinib treatment in mouse models. It is suggested that

lymecycline inhibited the resistance of the cell cycle to EGFR-TKI and induced apoptosis in NSCLC by inhibiting EGFR phosphorylation and GRB2-mediated AKT/ERK/STAT3 signaling pathways. Growth factor receptor-bound protein 2 (GRB2) is an EGFR-binding adaptor protein essential for EGFR phosphorylation and regulation of AKT/ERK/STAT3 signaling pathways. Lymecycline targeted GRB2 and inhibited the resistance of the cell cycle to EGFR-TKI, arresting disease progression, and inducing apoptosis in cancer cells.

According to experts at VulcanChem, lymecycline is a semisynthetic derivative of tetracycline and is approximately 5000 times more soluble along with being unique among tetracyclines. It is considered as a broad-spectrum second-generation tetracycline antibiotic used for the treatment of acne and other susceptible bacterial infections. Lymecycline binds to the 30S ribosomal subunit, preventing amino-acyl tRNA from binding to the A site of the ribosome, which prevents the elongation of polypeptide chains. This results in bacteriostatic actions, treating various infections. Lymecycline is lipophilic and easily crosses the cell membrane and passively diffuses through bacterial porin channels. In general, tetracycline cytotoxicity induces apoptosis in lymphocytes, osteosarcomas, and prostatic cancers and may prevent metastasis.

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