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Drug development for EGFR-TKI resistance in non-small cell lung cancer cells: Novel dual inhibitor of EGFR and cMET

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Lung cancer is the leading cause of cancer-related death worldwide with a 5-year survival rate of less than 15% globally, accounting for more than 1.4 million deaths per year. Lung cancer is one of the most heavily mutated and gnomically altered cancers. Despite the longer progression free survival of patients with TKI-treatment a high proportion eventually develop resistance. Resistance to targeted therapies is generally classified as either primary (i.e., intrinsic) or secondary (i.e., acquired). This approach has been variously termed "personalized cancer medicine", "individualized cancer medicine" or "high precision cancer medicine". Chemical synthesis led to further compound evaluations that revealed increased biochemical potency. The earliest efforts to utilize molecular profiling of tumors to guide more precise therapies for individual patients have met with remarkable success. Epidermal growth factor receptor-tyrosine kinase inhibitors (EGFRTKIs) show a clinical benefit when used to treat patients with EGFR-mutated non-small cell lung cancer (NSCLC), but this treatment unfortunately fails in patients with TKI-resistant tumors. We here provide evidence that NSC777201 (N19), a novel dual inhibitor of EGFR and cMET, efficiently overcomes the EGFR-TKI resistance in EGFR-mutated NSCLC cells *via* simultaneous degradation of both proteins by ubiquitin-proteasomes. In summary, N19 may act as a novel dual inhibitor of EGFR and cMET that induces apoptosis in TKI-resistant EGFR-mutated NSCLC cells and suppresses xenograft tumor formation. We suggest that N19 may be a potential new-generation TKI or HSP90 inhibitor used for treatment of NSCLC patients who show resistance to current TKI targeting therapies.

Biography

Hsu-Shan Huang has completed his Dr. rer. nat. from Regensburg University, Germany and Pharmaceutical studies from NDMC School of Pharmacy. He was the Dean of School of Pharmacy and Director of R&D, NDMC. He has published more than 95 SCI papers and 30 patents in reputed journals and has been serving as an Editorial Board Member of repute.

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