Topical Vitamin K3 (Menadione) Prevents Erlotinib and Cetuximab-Induced EGFR Inhibition in the Skin

Roman Perez-Soler,1 Yiyu Zou,1 Tianhong Li,1 Maomi Li,2 Wancai Yang,1 Carmen Tornos,3 Yi-He Ling1
1Department of Oncology, 2Department of Pathology, Albert Einstein College of Medicine, Bronx, NY; 3Department of Pathology, State University of New York at Stony Brook, NY

Methods and Results

Exogenous ligand EGF fails to rescue the inhibitory effect of erlotinib on pEGFR.

EGF rescues EGFR TK function in A431 cells treated with cetuximab but not small molecule EGFR TKI erlotinib

Vitamin K3 (menadione) is a reversible phosphatase inhibitor that activates EGFR tyrosine kinase.

Vitamin K3 (VK3) is a strong activator of the EGFR pathway in A431 cells

VK3 prevents EGFR inhibition by erlotinib in A431 cells

VK3-induced EGFR activation is reversible in A431 cells

Conclusions

1. Vitamin K3 (menadione) is a phosphatase inhibitor and an EGFR TK activator
2. VK3 can rescue EGFR TK function in A431 cells treated with cetuximab and the small molecule EGFR TK inhibitor erlotinib
3. EGFR can rescue EGFR TK function in cells treated with cetuximab but not in cells treated with small molecule EGFR TK inhibitors
4. Topical VK3 is an EGFR activator in the skin of nude mice and rescues EGFR TK function in mice treated with oral erlotinib

Future Directions

Development of a topical Vitamin K3 formulation and clinical testing for the treatment of EGFR Inhibitor-induced skin rash.