

PI3K/AKT/GSK-3 β signaling pathway involving in the mechanism of polymyxin B induced melanogenesis

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Abstract

Backgrounds: Polymyxin B, which is a last line antibiotic for multi-drug resistant gram-negative bacteria, has been reported to induce skin hyperpigmentation in patients during treatments. 8~15% or more cases were reported hyperpigmentation, especially in head and neck, seriously influencing the compliance of patients. To investigate the mechanism of hyperpigmentation is beneficial for intervention strategy and improve compliance. **Methods:** The melanoma cells, SK-MEL-2 cells were employed in the present study to verify whether polymyxin B treatment could directly induce hyperpigmentation. Melanin contents were measured by hot alkali lysis method and tyrosinase were quantified by dopaquinone oxidation method. The real-time quantitative PCR was applied to measure the mRNA levels of melanogenesis-related genes to investigate the possible signaling pathway involved in the polymyxin B induced hyperpigmentation. **Results:** The melanin content and tyrosinase activity were up-regulated after 5 μ g/mL polymyxin B treatment in SK-MEL-2 cells at 48 hr. and 72 hr. The mRNA levels of melanogenesis-related genes were up-regulated, including PI3K, Akt, GSK-3 β , CREB, MITF in the polymyxin B treatment group compared with control group at 48 hr. ($p < 0.001$). **Conclusions:** In the present study, for the first time to reveal that polymyxin B induced hyperpigmentation involved the signaling pathway of PI3K/AKT/GSK-3 β and the up-regulation of CREB and MITF subsequently, then induced the activity of tyrosinase and melanin content in melanoma cells.

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