EDITORIAL

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Identifying and overcoming rituximab resistance in diffuse large B-cell lymphoma using next-generation sequencing

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Rituximab is a monoclonal antibody that targets the CD20 B-cell antigen and is the standard first-line treatment for diffuse large B-cell lymphoma (DLBL). However, a significant proportion of patients with relapsed or refractory DLBL are resistant to rituximab [1].

Jeon et al. [2] provides new insight into the mechanisms of rituximab resistance in DLBL and identifies a potential therapeutic strategy for overcoming this resistance. The authors developed a rituximab-resistant cell line (RRCL) by sequentially exposing cells to increasing concentrations of rituximab and then performed next-generation sequencing (NGS) to identify differences in gene expression between the RRCL and a rituximab-sensitive cell line.

The NGS results showed that genes related to the mitogen-activated protein kinase (MAPK) signaling pathway were activated in the RRCL. Western blot analysis revealed that phospho-38 protein expression increased in the RRCL, suggesting that p38 MAPK activation was associated with rituximab resistance. These results agree with previously published findings asserting the critical involvement of the MAPK signaling cascade in the onset of DLBL. Recent research has shown that the p38-MAPK pathway is a major driver of rituximab resistance in DLBL. P38 MAPK is a signaling molecule that plays a role in cell survival, growth, and migration. Activation of p38 MAPK is associated with rituximab resistance in DLBL [3].

The authors also found that the orally administered iron chelator deferasirox [4] has a synergistic effect with rituximab in killing RRCL cells [5]. This suggests that activation of p38 MAPK may be a key driver of rituximab resistance and that inhibiting p38 MAPK with deferasirox may be a promising approach to re-sensitizing DLBL cells to rituximab.

This study significantly advances our understanding of rituximab resistance in patients with DLBL. The findings suggest that deferasirox may be a promising therapeutic agent for overcoming rituximab resistance in DLBL patients. However, additional clinical research is needed to validate the findings and to determine the optimal dose and deferasirox schedule combined with rituximab. The results provide a rationale for further research into the use of p38 MAPK inhibitors, such as deferasirox, to overcome rituximab resistance in DLBL patients.

Strengths

The authors used a well-designed experimental approach to identify differences in gene expression between rituximab-sensitive and rituximab-resistant DLBL cells.

The findings are consistent with previous studies showing that p38 MAPK activation is associated with rituximab resistance in DLBL.

The results suggest that deferasirox may be a promising therapeutic agent for overcoming rituximab resistance in DLBL.

Limitations

The study was conducted in a preclinical setting using cell lines. Therefore, additional clinical trials are needed to validate the findings.

The optimal deferasirox dose and schedule for overcoming

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rituximab resistance in DLBL patients must be determined.

Overall, deferasirox is a promising new therapeutic agent for DLBL patients. However, additional clinical research is needed to fully define its role in the treatment of DLBL. Still, the available data suggest that it has the potential to improve outcomes in patients with this aggressive form of lymphoma.

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