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mTOR expression in acute lymphoblastic leukemia: Possible contribution of mTOR in predicting response to induction chemotherapy

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Introduction: With comprehensive treatment protocols available, overall survival across all risk groups is attained in 50% cases of ALL (acute lymphoblastic leukemia). Survival in childhood ALL has markedly improved to 80% however, limited success is achieved in adults. Disease recurrence is seen most often in adults contributing to their poor prognosis. Furthermore, among the two subtypes of ALL, relapse is more prevalent in T-ALL compared to B-ALL. Therefore, it is imperative to explore new distinguished targets in ALL for improving treatment outcome. In ALL, limited data is available on mTOR gene expression in clinical samples and its role in predicting response to induction chemotherapy.

Methodology: mRNA expression of mTOR was determined quantitatively by Real Time PCR in 50 ALL patients (30 B-ALL and 20 T-ALL) and correlated with response after induction chemotherapy.

Results: Expression level of mTOR was upregulated in more than 50% of cases of ALL. In T-ALL, high mTOR was commonly seen more in adults than children (82% vs 55% cases) while in B-ALL it was same (~ 63% cases) in both children and adults. Mean fold change of mTOR expression was significantly higher in non- responders compared to responders of both adult B-ALL (7.5 vs. 2.7, p=0.05) and T-ALL (13.9 vs 2.4, p=0.001). Similar results were seen in childhood non-responders when compared to responders of both B-ALL (14.5 vs. 2.5, p=0.006) and T-ALL (24.2 vs 1.7, p=0.002). Interestingly, we observed that mTOR expression was two times higher in non-responders of children compared to adults in both B-ALL (14.5 vs 7.5, p=0.05) and T-ALL (24.2 vs 13.9, p=0.01). Multivariate analysis with known prognostic factors revealed that mTOR expression independently predicts clinical outcome in ALL.

Conclusion: This study demonstrates that high mTOR expression is associated with poor clinical outcome in ALL and can serve as a potential target for novel therapeutic strategies.

Biography

I am working in the field of hematological malignancies. I work closely with leukemia patients. My work includes flow cytometric diagnosis of acute leukemia. The project is aimed at elucidating the role of mTOR in acute lymphoblastic leukemia etiology and chemotherapeutic drug resistance.

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