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| 学位論文の題名 | CCR4 mutations associated with superior outcome of adult T-cell leukemia/lymphoma under mogamulizumab treatment  
（CCR4遺伝子変異はモガムリズマブ（抗CCR4抗体）治療における成人T細胞性白血病/リンパ腫の良好な予後と関連する）  
Blood 2018;132:758-761 |
| 論文審査担当者 | 主査：山崎 小百合  
副査：高橋 智，稲垣 宏 |
Title:
CCR4 mutations associated with superior outcome of adult T-cell leukemia/lymphoma under mogamulizumab treatment

ABSTRACT

Adult T-cell leukemia/lymphoma (ATL) has a dismal prognosis. CCR4 is expressed by tumor cells from most ATL patients, so therapeutic antibodies such as mogamulizumab, may be effective treatments. Here, we investigate whether gain-of-function mutations in the carboxyl terminus of CCR4, which were observed in 38 (33%) of 116 ATL patients, influence overall survival (OS) and response to treatment. We found no significant differences in OS when the whole patient cohort was stratified according to CCR4 mutations. However, in those receiving mogamulizumab, 5-year survival from initiation of treatment in patients with (n = 11) or without (n = 31) CCR4 mutations was 72.7% and 26.2%, respectively (P = 0.027). In contrast, CCR4 mutations did not influence the outcome of allogeneic hematopoietic stem cell transplantation. Finally, in patients with aggressive-variant ATL, 5-year survival on mogamulizumab for patients with (n = 10) or without (n = 28) CCR4 mutations was 80.0% and 24.7%, respectively (P = 0.006). These findings suggest that ATL patients with gain-of-function CCR4 mutations are especially good responders to mogamulizumab-containing treatments. Thus, we conclude that CCR4 gain-of-function mutations determine sensitivity to mogamulizumab therapy in ATL.