

主 論 文 要 旨

報 告 番 号	① 乙 第	号	氏 名	コ ウ レ イ カ
主 論 文 題 名 HSP90 promotes tumor associated macrophage differentiation during triple-negative breast cancer progression (HSP90はトリプルネガティブ乳がんの進行過程において腫瘍関連マクロファージの分化を促進する)				
(内 容 の 要 旨) Tumor-associated macrophages (TAMs) originating from monocytes are crucial for cancer progression; however, the mechanism of TAM differentiation is unclear. We investigated factors involved in the differentiation of monocytes into TAMs within the tumor microenvironment of triple-negative breast cancer (TNBC). We screened 172 compounds and found that a heat shock protein 90 (HSP90) inhibitor blocked TNBC-induced monocyte-to-TAM differentiation in human monocytes THP-1. TNBC-derived conditional medium (CM) activated cell signaling pathways, including MAP kinase, AKT and STAT3, and increased the expression of TAM-related genes and proteins. These inductions were suppressed by HSP90 inhibition or by knockdown of HSP90 in TNBC. Additionally, we confirmed that TNBC secreted HSP90 extracellularly and that HSP90 itself promoted TAM differentiation. In a mouse tumor model, treatment with an HSP90 inhibitor suppressed tumor growth and reduced TAMs in the tumor microenvironment. Our findings demonstrate the role of HSP90 in TAM differentiation, suggesting HSP90 as a potential target for TNBC immunotherapy due to its regulatory role in monocyte-to-TAM differentiation.				