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Oral ingestion of Lentinula edodes mycelia extract inhibits B16 melanoma growth via mitigation of regulatory T cell-mediated immunosuppression.

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Source

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Abstract

Mitigation of regulatory T cell-mediated immunosuppression is crucial for optimal in vivo anti-tumor immune responses. In this study, we examined the anti-tumor effect induced by oral ingestion of an immunomodulating diet comprised of Lentinula edodes mycelia (L.E.M.) extract. C57BL/6 mice were inoculated subcutaneously in the footpad with B16 melanoma and fed L.E.M. extract. Ingestion of L.E.M. extract significantly inhibited tumor growth, and this in vivo anti-tumor effect was not observed in nude mice, suggesting a T cell-dependent mechanism. In addition, ingestion of L.E.M. extract led to significant restoration of H-2K(b) -restricted and melanoma-reactive T cells in the spleen and draining lymph nodes of melanoma-bearing mice. Flow cytometry analysis revealed that the percentage of Foxp3(+) CD4(+) T cells increased in spleen and draining lymph nodes in melanoma-bearing mice, but decreased significantly with ingestion of L.E.M. extract. Importantly, selective depletion of CD8(+) T cells abolished the L.E.M.-induced anti-tumor effect, whereas that of CD4(+) T cells or CD25(+) cells showed no additive influence on the effect. Real-time PCR analysis revealed that ingestion of L.E.M. extract by melanoma-bearing mice decreased the level of Foxp3 mRNA within the tumor tissues, and lowered plasma transforming growth factor (TGF)-β. Furthermore, an in vitro assay revealed that an immunosuppressive activity of CD4(+) T cells from melanoma-bearing mice was canceled by ingestion of L.E.M. extract. Our results indicate that oral ingestion of L.E.M. extract restores immune responses of class I-restricted and melanoma-reactive CD8(+) T cells in melanoma-bearing mice, presumably by a mitigation of regulatory T cells-mediated immunosuppression.

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