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"DRRK2: A novel Therapeutic Target for Multiple Myeloma"

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SCIENTIFIC ABSTRACT
Dependency on ubiquitin-proteasome system is the "Achilles' heel" of multiple myeloma. We identified a kinase (DYRK2), which directly phosphorylates the proteasome and dramatically upregulates proteasome activity. We demonstrated that blocking DYRK2-mediated proteasome phosphorylation impaired proteasome activity, leading to dramatic reduction of myeloma burden in mouse xenografts. We further identified a potent and selective DYRK2-inhibitor, which markedly sensitized all multiple myeloma cell lines (including bortezomib resistant lines) to proteasome inhibitor with no significant effect on non-cancerous myeloid cells and reduced mouse tumor burden. Herein, we report a novel kinase, which serves as a promising drug target to alleviate myeloma burden in patients.