

Pharmacology of Immunosuppressive Drugs

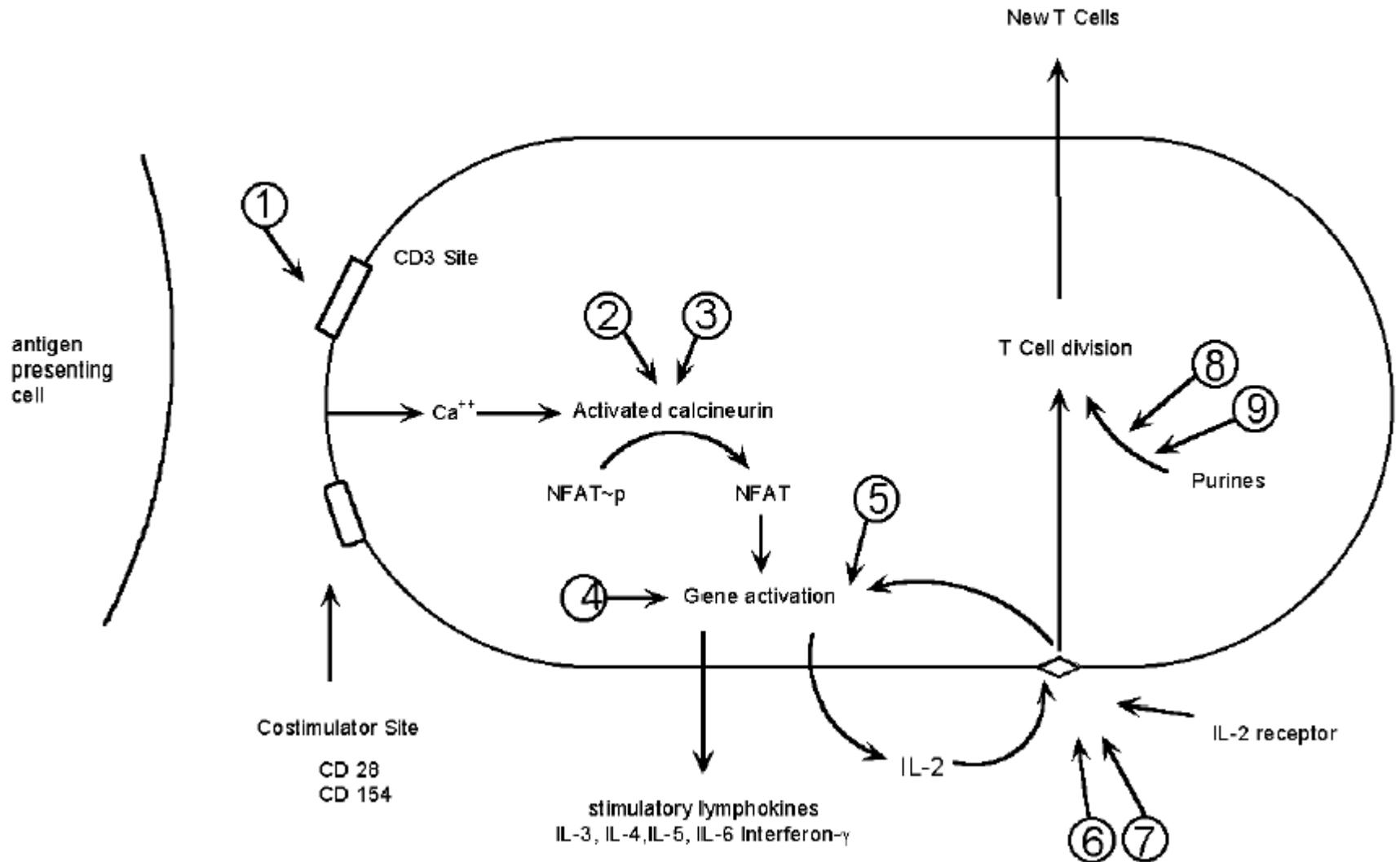
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CORE General Surgery RPAC

Site of action of T cell immunosuppressants



#	Drug	Mechanism	side effects
1	orthoclone OKT3	monoclonal mouse antibody directed against the CD3 site of the T Cell	first dose effect causing cytokine release syndrome- fever, pulmonary edema, seizures. Can be prevented by pretreatment with glucocorticoid
2	cyclosporine	binds to cyclophyllin. The cyclosporin-cyclophyllin complex inhibits the activation of nuclear factor of activated Tcells (NFAT), which prevents transcription of IL-2. Neoral is a newer formulation which has better bioavailability and is more predictably absorbed.	nephrotoxicity, hepatotoxicity, hypertension, hypercholesterolemia, hirsutism, gum hyperplasia
3	tacrolimus	binds to nrbf-12. The complex then inhibits NFAT activation.	Nephrotoxicity, neurotoxicity, alopecia, diabetes
4	corticosteroids	binds to cytosolic receptor, migrates to nucleus, binds to glucocorticoid receptor elements on the gene.	Inhibits all immune function, alters metabolism, suppresses adrenal axis, etc.
5	sirolimus	inhibits activation of rapamycin, a kinase which is required for the binding of IL-2-induced binding factors to the nucleus. Inhibits secretion of a variety of activating factors. Used in conjunction with cyclosporin and glucocorticoids.	decrease WBC, Increase triglycerides
6	daclizumab	humanized monoclonal antibody directed against the IL-2 receptor on T cells	?
7	basiliximab	mouse/human monoclonal chimeric antibody directed against the IL-2 receptor.	?
8	azathioprine	a prodrug metabolized to 6-mercaptopurine. It inhibits de novo synthesis of purines by activated T cells	gi upset, bone marrow depression, rash
9	mycophenolate mofetil	prodrug converted to mycophenolic acid, which inhibits inosine monophosphate dehydrogenase, a step in the de novo synthesis of purines	gi, bone marrow depression

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