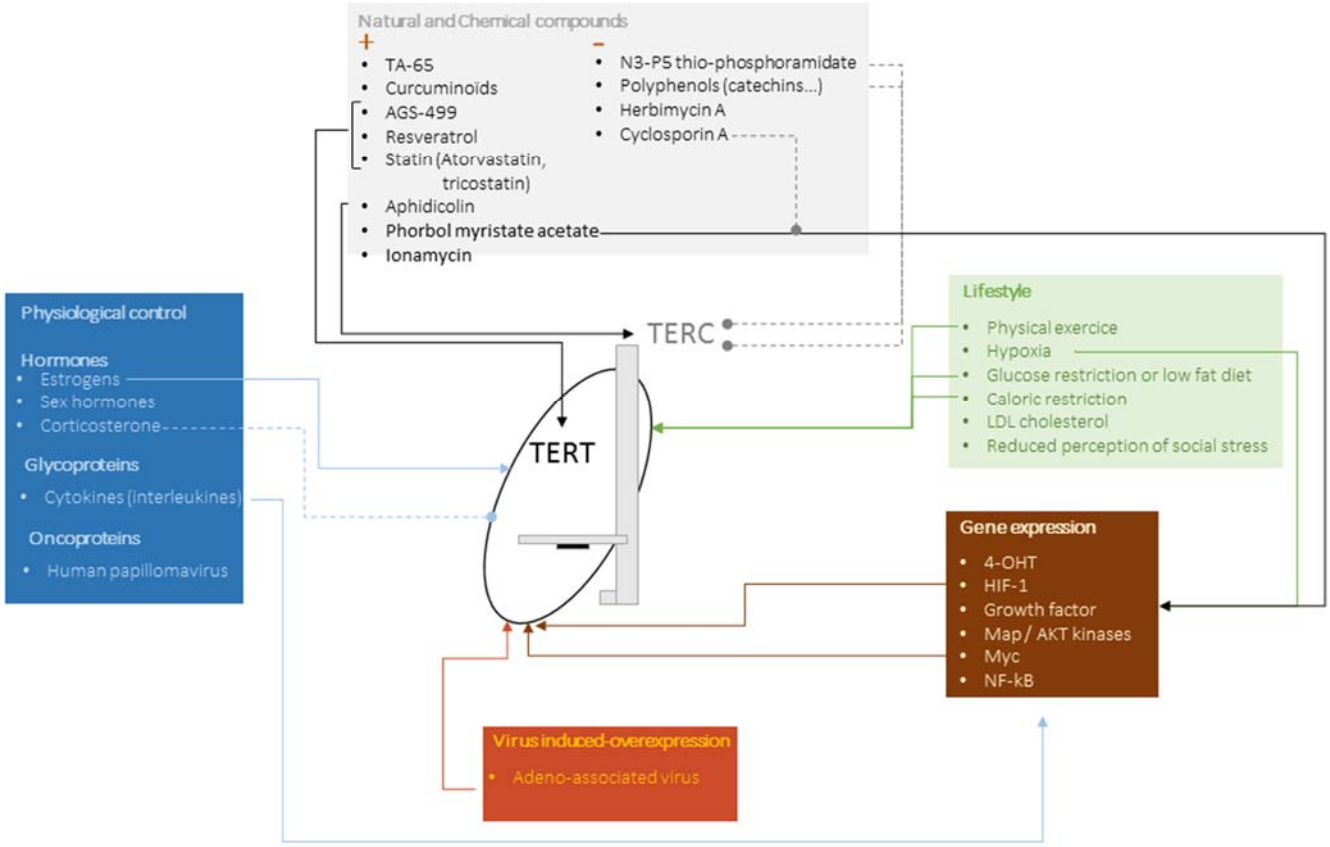
Box 3: Families of currently known *in vivo* modulators of telomerase activity.



Colored boxes represent five candidate categories for telomerase modulation, via natural and chemical compounds; lifestyle; gene expression; virus-induced overexpression; or physiological control. Arrows indicate when the specific activation effect is known to be mediated through TERC (RNA) or TERT (protein) components of telomerase. Plain arrows highlight pathways of activation impact while dashed arrows underline inhibition impact pathways. Most of the activation pathways are related to TERT – AGS-499 [1]; Resveratrol [2, 3]; Statin [4]; physical exercise [5]; dietary restriction [6] but see [7]; adeno-associated viruses [8]; and estrogens [9]; phorbol myristate acetate [10]; hypoxia [11]; and cytokines [12] – , whereas only aphidicolin has been shown to activate TERC [13]. Polyphenols [14] and N3-P5 thio-phosphoramidate [15] both inhibit TERC while corticosterone has an inhibitory effect on TERT [16]. Cyclosporin A has an inhibitory effect on the phorbol myristate acetate pathway [10].

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