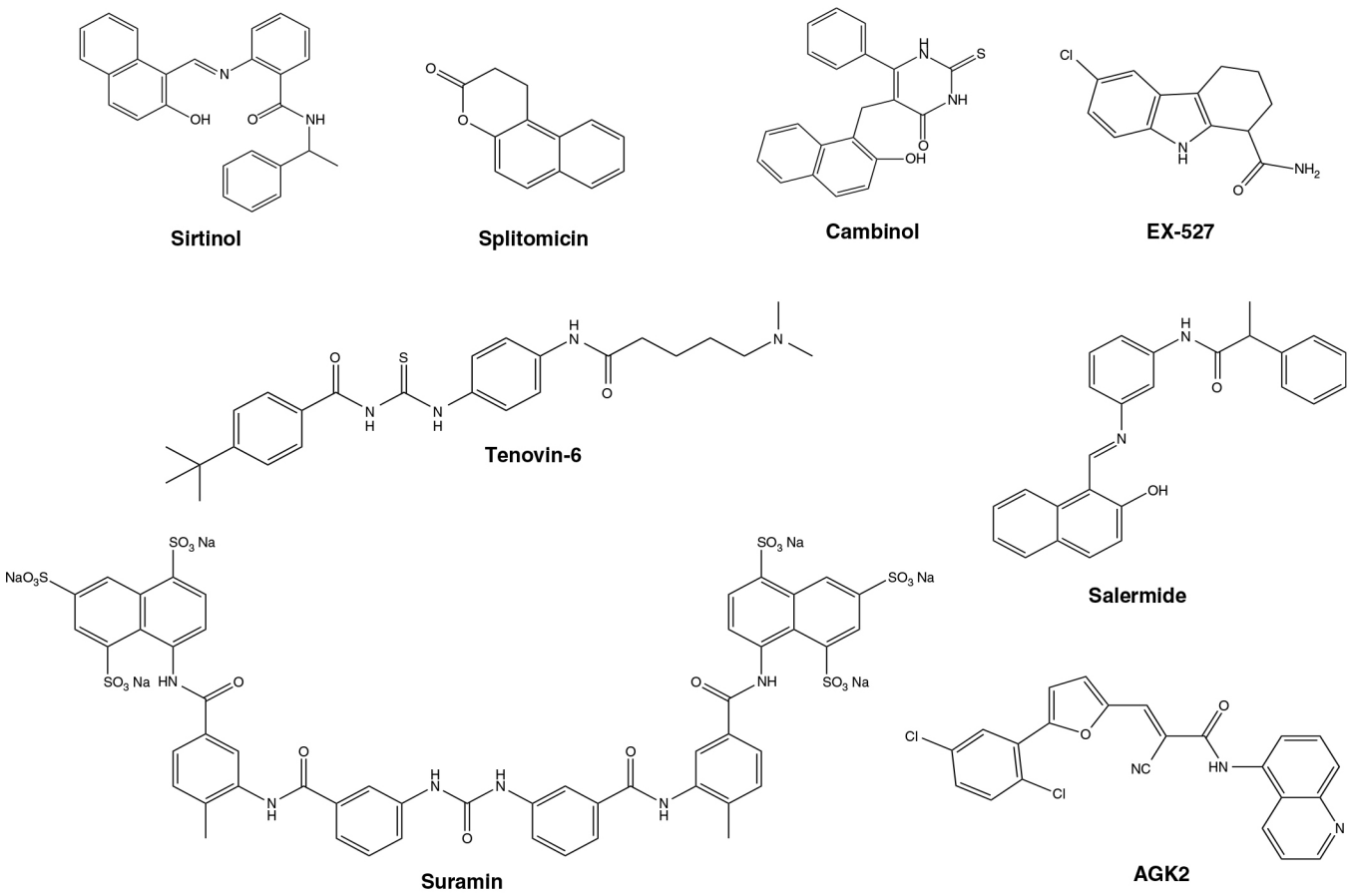

Figure 10. Sirtuin inhibitors. Sirtinol and splitomicin are identified as the first small molecule sirtuin inhibitors that affect telomere silencing in yeast. Cambinol is a splitomicin-related β-naphthol that is more stable than splitomicin and increases p53 acetylation showing antitumor activity in BCL6-expressing Burkitt's lymphoma. Salermide was designed based on the structure of sirtinol by molecular modeling and inhibits both SIRT1 and SIRT2 more effectively than sirtinol. Tenovin-1 and its water-soluble analog tenovin-6 induce p53 acetylation; their cellular targets were determined to be SIRT1 and SIRT2. A high-throughput screen revealed a number of indole compounds including EX-527, which selectively inhibits SIRT1 over SIRT2. Kinetic analysis suggests that EX-527 binds to the nicotinamide-binding site. AGK2, which was reported as a SIRT2 selective inhibitor, shows more than 10-fold selective inhibition relative to SIRT1 and SIRT3. Suramin, which was originally developed for treating trypanosomiasis and onchocerciasis, inhibits the NAD^+-dependent deacetylase activity of sirtuins by inducing sirtuin dimerization.