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Validation of Fluorimetric Assay of Histone Deacetylase for Inhibitors from Plant Origin

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Histone deacetylase inhibitors (HDACi) have received high interest as anti-cancer agents recently. HDACi may influence tumor growth by an inhibition of angiogenesis as well as by increasing tumor cell immunogenicity [1]. In many clinical trials the effect of several HDACi on different tumors are studied at the moment [2].

The purpose of this work has been to improve and validate an in vitro HDAC assay for high throughput screening (HTS) of plant extracts. A fast method for the determination of HDAC activity and the identification of potent natural product-based inhibitors of HDAC activity has been established. Nuclear cell extracts from HUVECs, VSMC and HeLa served as source of the HDAC protein. Natural compounds were selected according to their structural relationship to known HDACi. The initial results showed that compounds such as several isoflavones, anthraderivatives and capsaicinoids have the potential to inhibit HDAC activity, although at micromolar concentrations. Further investigations aim at finding natural HDACi effective at nanomolar concentrations.

In conclusion, the modified HDAC assay is well suited to HTS efforts for the screening of plant extracts, fractions and natural compounds for new HDACi and thus in the development of new drugs. The assay system combines high sensitivity, speed and effectiveness for plant extracts. The HDAC assay is well-suited for our approach and the results have been confirmed by another test system.

[1] Ogbomo H, Michaelis M, Kreuter J, Doerr HW, Cinalt J Jr. Histone deacetylation inhibitors supress natural killer cells cytolitic activity. FEBS Letters 2007; 581, 7: 1317–1322. doi:10.1016/j.febslet.2007.02.045

[2] Garber K. HDAC inhibitors overcome first hurdle. Nature Biotechnol. 2007; 25, 1: 17–19. doi:10.1038/nbt0107-17