Chemical Genomics Based Target Identification of Natural Products

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Hundreds of natural products are discovered every year in hopes of curing human diseases. In most case, however, natural products are hard to be utilized as therapeutic drugs directly because of their side effects and insufficient mode of actions study. Nevertheless they have powerful potential to be developed as biochemical agents as well as lead compounds for clinical drug development. By combination of cut-in-edge technologies of chemistry, biology, and genomics, natural products or failed drugs with interesting biological activities but having little studies on target proteins as well as mode of actions could be re-illuminated as potential candidates for novel drugs R&D. The target identification of natural products plays important role for this purpose and several target proteins of natural products have been identified (e.g., FK506: FKBP, taxol: tubulin, mevalotin: HMG-CoA reductase, TNP470: methionine amiopeptidae II, FK228, depudecin: histone deacetylase, radicicol: Hsp90, ·).

We have applied this idea to identify the target protein of natural products having anti- angiogenenic activity. From both *in vitro* and *in vivo* assays for angiogenesis, several chemicals with different structure have been isolated from our lab recently. Those are curcumin from oriental herbal medicine and acalycixenolide E (AX-E) from a marine organism, respectively. These structurally unrelated compounds show potent anti-angiogenic activities as one of their biological activities but their cellular target proteins have not been identified yet. The strategies of affinity matrix- or DNA microarry-based target identification for each chemical has been used and the data will be presented. Target identification using chemical genomics approach will provide novel targets for the development of anti-angiogenesis therapy and help to decipher the molecular mechanism of angiogenesis.

References

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