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Letter to the Editor Open Access

Bioactive Molecules: Translating Chemical and Biological Information from Yeast through Arabidopsis to Crops

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Letter to the Editor

Chemical tools have been extensible used to probe complex biological processes [1]. A variety of small molecules (<500 Da) like Brefeldin A, Tyrphostin A23, Wortmannin have been intensively utilized to study endomembrane protein trafficking and have illustrated corresponding biological functions [2-7]. After the application, bioactive small molecules can be rapidly permeated or transported into cells to create observable effects. These molecules can be washed out to reverse their effects, permitting a return to a normal state. This rapid and reversible behavior along with precise concentration and time of treatment provides a high degree of control, permitting dynamic processes to be studied in vivo.

In the past decade several academic and company research initiatives undertook the systematic design and synthesis of small molecules (<500Da) and their subsequent use as probes for different biological processes in diverse organisms. As a result several collections of bioactive compounds, chemical libraries, became available for the research community. These libraries consist of low-molecular weight compounds synthesized by combinatorial chemistry with defined properties according to the Lipinski rule of five [8,9]. These rules outlines favorable physicochemical properties to get bioactive compounds, molecular weight (Da) ≤500, logP (octanol/water partition coefficient) ≤ 5, Number of H-bond donor ≤5, Number of H-bond acceptor ≤10, Rotatable bonds ≤12 [8]. Application of small bioactive molecules as a strategy to systematically screen for novel modifiers of a biological phenomenon of interest have gained increasing attention [10]. These approach, named chemical genomics, combines chemistry and biology along with bioinformatics which is required for data mining, structure analysis, data sharing and the extraction of useful data [11]. In principle, a chemical genomic screen can be performed in any system.

A chemical genomics high throughput screening (HTS) in Saccharomyces cerevisiae allowed to identify compounds that interfere with the delivery of the vacuolar resident protein carboxypeptidase Y (CPY) [12]. Among those compounds was selected Sortin2. Structure-activity relationship (SAR) studies identified active and inactive homologs of this compound (Norambuena et al.,). Sortin2 contains a chlorobenzene, a furan, a thiazolidine ring, and a sulphite group. The sulphite group was essential to the activity of the compound. The data suggest that the interaction between Sortin2 and its target most likely requires a dense electron cloud to affect the target activity and function [13].

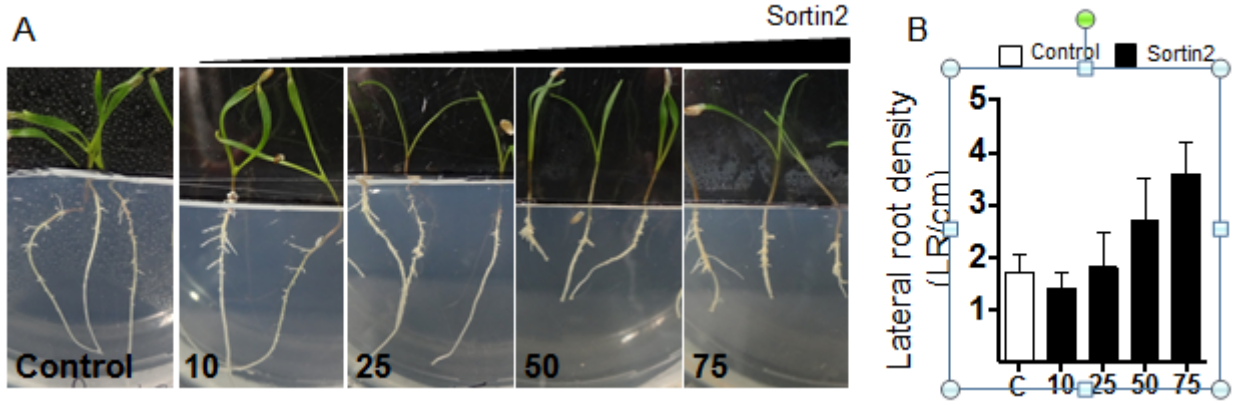

Figure 1: A compound identified by chemical genomics modifies root system architecture in carrots. 7 day-old carrot seedlings were transferred to Control and different concentrations of Sortin2 (10 to 75 µg/mL). A. Whole plant images of carrot seedlings after seven days of Sortin2 treatment. B. Lateral root density quantification of control and Sortin2 treated plants. mean + SEM. N=6.

Sorting2, was also capable to interfere with the delivery of the vacuolar of CPY in the model plant Arabidopsis [12]. Interestingly in this plant Sortin2 modifies the root architecture increasing lateral root occurrence and inhibiting principal root growth increasing overall lateral root density (LRD) [14]. An increase in LRD is a desirable trait in crops as it optimizes water and nutrient uptake. Thus, translating all

the chemical and biological information available for Sortin2 could be effective to improve crop yields. We examined Sortin2 effect in carrot (Daucus carota). Carrots are characterized by a strong, deep, well-developed root system. Lateral root development throughout is very poor [15]. A dry surface soil tends to promote a vigorous development of strong laterals roots from the deeper portions of the root. Thus, generating more lateral root would be a desirable trait to overcome stress. We tested the modification of carrot roots by means of chemical stimulation with Sortin2. Roots of seven day-old seedlings were exposed to Sortin2 for additional seven days. Aerial organs of Sortin2-treated plants did not showed color or turgor differences from control plants (Figure 1A). Meanwhile, root was strongly modified (Figure 1A). Figure 1B shows that the lateral root density was increased in a dose-dependent manner in Sortin2 treated plants. The highest Sortin2 concentration tested, 75 µg/mL, trigger a two-fold increase in lateral root density.

These results indicates that chemical information and action can be translated from yeast through model plants as Arabidopsis and ultimately to crops. We emphasizes on the critical role that chemistry is playing in unraveling physiological processes in plants, and how these new insights allow to suggest novel approaches to improve yield in crops.

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