Using in-house validated chemical reactions that are suitable for parallel synthesis and a collection of multifunctional „drug-like" scaffolds, a dedicated discovery screening library of 10,000 compounds has been enumerated by a cascading diversity building approach (www.amriglobal.com). Based on the cytotoxicity measured in MRC-5 human fibroblast assay, further on HepG2 human hepatocarcinoma assay and the interpolated IC_{50} values, 668 compounds were selected aiming for maximal diversity of scaffolds.

These selected 668 small, drug-like compounds of unknown effects and other, toxic compounds of known and of yet unknown effects and pharmaceutical active entities were screened for their gene expression profiles *in vitro*, over 56 selected biomarkers (toxicology, transporters). Our objective was to see to what extent the highly similar chemical structures induce similarities in their hepatotoxic fingerprints and to test the analytical performance of the nanocapillary QRT-PCR technique and its general applicability for the field of toxicogenomics.

Preliminary tests have been performed with our inhouse ToxicoScreen DNA-microarrays (Vass et al. 2006) and with the traditional QRT-PCR technique, following which we shifted to the OpenArray nanocapillary quantitative real-time PCR-technology (Morrison et al. 2006; Avidin Ltd.-BioTrove Inc.) that has meanwhile appeared on the market. This later technology merges the high-throughput of DNA-microarrays with the sound characteristics of QRT-PCR.

By the combination of a relatively large combinatorial chemical library and a relatively small set of selected toxicological biomarkers, we intended to avoid the two culprits of toxicogenomics: 'the curse of dimensionality' (too many genes), and 'the curse of dataset sparsity' (too few samples). The generally accepted, however rarely adapted sample-per-feature ratio for robust clustering performance is at least 5 to 10.

Based on the scaffold structure or the characteristic residues, we assigned the tested chemicals into subgroups. Different clustering methods were applied, based on results from unsupervised hiearchical clustering we performed supervised, K-means clustering. Our objective was to see wether the correlation between gene expression fingerprint and structure of the compound inducing it can be detected and to what extent can this correlation be rooted back to the scaffolds.

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Tools for improving stress adaptation in cereals

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Abiotic stresses are very important factors that reduce crop productivity. Plant root is the primary organ for uptake of water and nutrients, therefore it plays important role in tolerance to stresses like drought or salinity. Plants developing stronger and deeper roots suffer less from water deficit. The aim of our work was to improve the stress-tolerance in cereals using transcriptome analysis of rice cultivars under drought stress conditions, and stress-induced and root-specific promoters.

Genes facilitating development of efficient root system can increase the survival of the plant. Fusions of drought stress-related root-specific promoters to these genes may provide environment friendly and efficient solution to improve roots of crop plants under stress conditions.

Based on published data two candidate promoters were selected: the rice *CatB* and the *RSOsPR10* promoters. The *CatB* promoter is known to be root-specific (Iwamoto et al. 2004), the expression of the *RSOsPR10* mRNA is high in salt and drought stress conditions in root (Hashimoto et al. 2004). Both promoters have stress-related transcription factor binding sites and (MYB, WRKY, DREB, LTRE) in their sequence. The 1.6 kb CatB promoter and the 2 kb of the 5` flanking region of the *RSOsPR10* were cloned, and fused to reporter genes. The constructs were transformed into rice calli and tobacco leaves.

On the regenerated T_0 rice plants, salt stress was performed that revealed the *RSOsPR10* promoter directing root-specific and stress-induced expression pattern of GFP reporter. CatB::GUS transformed T_0 and T_1 tobacco plants showed root and vascular bundle-specific GUS expression, and induction under salt stress.

The changes of the rice root transcriptome under stress conditions and its alterations during a daytime period were investigated in a greenhouse experiment including three cultivars growing in a sand-perlite soil mixture. The stressed plants were irrigated with 20% of water for one month, causing drought-stress condition. The samples were collected three times in a day from each genotype both from drought stressed and control.

To follow the transcriptional changes, root samples from the most tolerant genotype were hybridized with rice oligonucleotide DNA chip. 3200 of the genes represented on the chip gave signal in all of the hybridizations, and 11.6% were up-regulated, and 6.7% were down-regulated in the adaptive cultivar.

Based on the expression profiles of genes during the day under drought-stress, eight clusters were built, and functional categorization was done based on the known or putative function of the encoded proteins, following the classification established by Yang et al. (2004).

Comparing the ratios of the gene-classes between the induced and repressed genes four groups showed significant difference in favor of the up-regulated genes. The ratio of the genes encoding proteins involved in metabolism, signal transduction and cell growth was higher among the induced genes.

To validate the results of the chip-hybridization, and to find stress-induced and root-specific genes, quantitative real-time PCR experiments were performed. Seven genes were tested, and the chip-hybridization results were confirmed for four of them: an *ABA/WDS induced* gene, a *LEA group 3*, a putative *LEA*, and a gene with unknown function. Furthermore, these genes` expression levels were determined in the shoot samples in all of the three genotypes. The alterations of the expression patterns reflected the differences in the stress-tolerance of the three cultivars. However all of them showed higher induction in roots than in shoots, the *LEA group 3* gene appeared to be the most stress-inducible and root-specific, becoming a candidate to develop expression cassettes including this gene.

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The study of the Nimrod protein and gene cluster in *Drosophila melanogaster*

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Every multicellular organism has to maintain its homeostasis in masses of invading microbes in its environment. The innate immunity constitutes the first line of defence against this challenge. As the defence mechanism of *Drosophila melanogaster* consists of innate immune processes only, lacking an adaptive immune system, it can be characterised as a less complex homologue of its mammalian counterpart, making the fruit fly a valuable model organism for studying innate immune responses.

The circulating blood cells of the fruit fly are key effectors of its immune defence. These hemocytes can be divided into three characteristic types. In wild type third instar larvae 97% of all circulating hemocytes are plasmatocytes, but even though it is the most abundant cell type in circulation, previously it could only be characterised based on its phagocytic capacity.

Our group identified the first plasmatocyte-specific immunological marker. After screening thousands of candidate hibridoma clones, we found two specific monoclonal antibodies, recognising different epitopes on the same molecule. We purified the antigenic protein, and analysed it with MALDI-TOF. A protein was identified with characteristic domain structure, containing a signal peptide, a CCxGY motif, EGF repeats, one transmembrane and an intracellular domain.

We have shown that the protein functions as a putative phagocytosis receptor of the plasmatocytes. As this protein helps the major sentinel cells catching bacteria we decided to name it after the big hunter Nimrod (*nimC1*; Kurucz et al. 2007b). The RNAi induced loss of function *nimC1* mutant plasmatocytes phagocytose *S. aureus* bacteria at significantly lower levels than the wild type, but *E. coli* phagocytic capacity was not compromised. On the other hand ectopic expression of the *nimC1* gene in S2 *Drosophila* cell line significantly enhanced the phagocytic capacity of cultured cells.

As it seemed that NimC1 is not the only phagocytosis receptor in *Drosophila*, we did in silico analysis searching for similar proteins in the fruit fly genome. Nimrod belongs to the superfamily of EGF repeat containing proteins, from which only 12 contain the characteristic CCxGY motif. In these proteins one or more EGF domains can be found, which fit a specific, more stringent consensus sequence, which we named NIM repeat. Nine of these genes, including *nimC1* can be found in a genomic region spanning 88 kilobase on the second chromosome. (Kurucz et al. 2007a; Somogyi et al.)

To prove, that these predicted genes are really transcribed, and to characterise their expression pattern we performed reverse transcription polymerase chain reactions using samples from whole third instar larvae, isolated hemocytes in wild type and hemocyte overproducing *l(3)mbn-1* mutant, and wild type adults.

All of the predicted genes were transcribed in every studied condition; the only exception was *nimA* which did not show any transcription activity in hemocytes.

In order to study the expression pattern of the *nimC1* homologues in more detail, we intend to produce new specific antibodies recognising the NimC1 homologue proteins. In order to acquire suitable amount of isolated protein for immunization, we have cloned the non-homologues regions of four different *nim* genes into prokaryotic expression vectors containing a HIS affinity tag, allowing isolation of the produced protein. In order to allow possible post-translational modifications of the expressed proteins, two of them are already cloned into affinity tagged eukaryotic expression vectors.