The method of gene expression analysis in complex morphological systems

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Investigation of gene expression level is a powerful approach in functional genetics. Analysis of expression is widely used in studies of tumors compared with normal tissues; mutant organisms compared with wild-type ones; organisms in different conditions and so on.

Usually the observed differential expression between samples being compared is presumed to be caused by the difference between samples (malignancy, mutation in certain gene). But in many cases the result of gene expression analysis contradicts data obtained with other methods (such as *in situ* hybridization or reporter genes) (Demidenko, Penin, 2012). In several cases this is a consequence of difference in morphology of compared objects. Various ratios of organs, tissues or cells cause observed differences in gene expression generating false positive results.

The methods of large-scale analysis of gene expression level such as microarrays or RNA-seq provide data about expression level of virtually all genes. We suggest the method that allows distinguishing between false positive results caused by difference in morphology of objects and truly differential expressed genes. This method is based on data which are provided by transcriptomic maps or other data about genes expression in different organs, tissues and cells.

We tested our method on two datasets (publicly available and own experimental data): *Arabidopsis thaliana* mutants with severe alterations in flower development and *Mus musculus* with bladder cancer (Wuesta *et al.*, 2012, Stone II *et al*, 2010). We found that 21.5% to 42.4% of differentially expressed genes are false positives; obviously, this significantly reduces the robustness of conclusions made on these data.

1. N.V. Demidenko, A.A. Penin (2012) Comparative analysis of gene expression level by quantitative real-time PCR has limited application in objects with different morphology, *PLoS One*, **7**(5):e38161.

2. S. E. Wuesta et al. (2012) Molecular basis for the specification of floral organs by APETALA3 and PISTILLATA, *PNAS*, **109**(33):13452–13457.

3. R. Stone II et al. (2010) Identification of genes correlated with early stage bladder cancer progression, *Cancer Prev Res (Phila)*, **3**(6):776–786.