Editorial

New Resources of Functional Genomics: Unique Vertebrate Models from Prague

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The Human Genome Project can be considered as the most significant scientific project of the twentieth century. The first draft of the complete human genome sequence, covering over 90% of 3 billion DNA base pairs, will be available in the summer 2000 (http://www.ornl.gov/hgmis/publicat/hgn/v10n3/01hgpdraft.html), and a comparable extent of the mouse genome will be ready by 2002 or 2003 (http://www.nih.gov/grants/guide/rfa-files/RFA-HG-99-001.html) as a result of concerted action of several sequencing centers in the world. Although the Human Genome Project will soon yield a complete catalogue of human genes with their position on the ultimate human genome map, the function of the majority of these genes will remain unclear. Thus, in the subsequent Functional Genomics phase of the Human Genome Project, the sequence information will have to be assigned to various normal and pathological functions at the whole-genome scale. The advancement of functional genomics will depend, among other things, on the availability of well-defined model organisms that can be genetically analyzed at will.

Genomes of several model organisms are intensively studied, including mouse, rat, zebrafish, frog, *Drosophila melanogaster* and *Saccharomyces cerevisiae*, (http://www.nih.gov/science/models/). The use of model organisms is manifold, including comparative genomics aiming to reveal conserved sequences, or providing models of human hereditary diseases. It was a paradox of classical genetics that the complex and quantitative phenotypes, such as predisposition to diseases, longevity, or sensitivity to infections, were practically inaccessible to detailed genetic analysis and identification of participating genes. In the recent years, the power of genetic analysis has been changing dramatically, and now it is possible to genetically dissect almost any phenotypic trait, from the predisposition to a particular cancer (Devereux and Kaplan, 1998), to fertility (Zidek et al., 1998) or behavior traits such as risk of alcoholism (Demarest et al., 1999) just to mention a few examples.

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Abbreviation: ENU – ethylnitrosourea.

One of the basic advantages of vertebrate models is the availability of unlimited numbers of genetically identical individuals in the form of inbred strains. With such models, any reproducible difference between two strains kept in the same environment is genetic in nature, and given the present functional genomics tools, it can be traced down to one or more differences in the sequence of the DNA strand. The current limitations of the non-human model organisms lie in the restricted repertoire of genetic polymorphisms and mutants simulating human genetic diseases. While the latter deficiency is being diminished in the mouse by large projects of ethylnitrosourea (ENU) mutagenesis with the dedicated centers in Germany, UK and the US, the restricted number of available alleles can be improved by wider use of inbred and congenic strains derived from unrelated founders.

In this issue, the locally developed inbred and/or congenic strains of mouse, rat and chicken are presented that have a potential to become a useful functional genomics resource. The mouse inbred strains PWD/Ph and PWK/Ph were derived at the Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, from the East European mouse sub-species, *Mus musculus musculus* (Gregorová and Forejt, this issue). Their main advantage is the high degree of genetic polymorphism caused by 1 million years of separate evolution from the *Mus musculus domesticus* genome, which represents the main component of the genomes of the commonly used inbred strains of laboratory mice. The large series of rat congenic strains (Křen et al., this issue) was derived from the SHR/Ola spontaneously hypertensive strain and normotensive BN-*Lx*/Cub progenitor strains to study hypertension and lipid metabolism. The production of the congenic strains was based on the previous development and analysis of the rat recombinant inbred strains (Pravenec et al., 1995; Křen et al., 1996), which are not presented here. The unique series of inbred and congenic strains of chicken (Plachý, this issue) were originally developed as a tool for immunogenetics (Plachý and Hála, 1997), but their potential is much broader, especially in the comparative genomics, due to their compact, 'puffer fish-like' genome.

References

Demarest, K., McCaughran, J. J., Mahjubi, E., Cipp, L., Hitzemann, R. (1999) Identification of an acute ethanol response quantitative trait locus on mouse chromosome 2. *J. Neurosci.* **19**, 549-561.

Devereux, T. R., Kaplan, N. L. (1998) Use of quantitative trait loci to map murine lung tumor susceptibility genes. *Exp. Lung. Res.* **24**, 407-417.

Křen, V., Křenová, D., Bílá, V., Zdobinská, M., Zídek, V., Pravenec, M. (1996) Recombinant inbred and congenic strains for mapping of genes that are responsible for spontaneous hypertension and other risk factors of cardiovascular disease. *Folia Biol. (Praha)* **42**, 155-158.

Plachý, J., Hála, K. (1997) Comparative aspects of the chicken immunogenetics (review). *Folia Biol. (Praha)* **43**, 133-151.

Pravenec, M., Gauguier, D., Schott, J. J., Buard, J., Kren, V., Bila, V., Szpirer, C., Szpirer, J., Wang, J. M., Huang, H., et al. (1995) Mapping of quantitative trait loci for blood pressure and cardiac mass in the rat by genome scanning of recombinant inbred strains. *J. Clin. Invest.* **96**, 1973-1978.

Zidek, V., Musilova, A., Pintir, J., Simakova, M., Pravenec, M. (1998) Genetic dissection of testicular weight in the mouse with the BXD recombinant inbred strains. *Mamm. Genome* **9**, 503-505.