considered to address the full potential of neural grafting in PD. Methodological changes could result in a completely different picture of the therapeutic value of neural grafting in PD and the scientific and clinical communities should be urged to display patience as grafting technology continues to be refined.

The review by Barker and Rosser also describes interesting novel sources of donor tissue that could be of use in transplantation therapy for PD. Different cell types are currently being investigated with the aim of generating as many dopaminergic neurons as possible and thereby making the neural grafting procedure more reproducible and available for a larger number of patients (Table 1).

Exciting research during the coming decade will reveal which cell type is most effective and then this can be applied in multiple centers worldwide as a true therapy for PD.

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The broader applications of uHTS ▲

The recent article by Julian Wölcke and Dirk Ullmann[1] in *Drug Discovery Today* describes the growing number and variety of tools available to enable researchers to fully realize the benefits of miniaturized ultra-high-throughput screening (uHTS). The article describes new homogeneous and heterogeneous/no-wash assays, plate types, detection technologies, and advances in robotics and data management. The availability of these new tools undoubtedly assures the increased use of high-density, miniaturized screening in the early phases of drug discovery. This will bring the intended benefit of streamlining the current target-to-lead paradigm of lead discovery. This is crucial to the drug discovery industry as the number of therapeutic targets will increase in coming years, as will the pressure to develop new drugs against these targets in an inexpensive and efficient manner.

As with all new technology, there are unexpected collateral benefits that arise beyond those originally intended. The uHTS technology described in the Wölcke and Ullmann article could have broader applications and influences on the drug discovery process. As the discovery of the genetic basis for disease progresses and the identification of new proteins continues, there are going to be many biological molecules and pathways whose role and function are unknown. An example is orphan G-protein-coupled receptors (oGPCRs) for which there is no known function, but an expected therapeutic role given the frequency that this receptor class plays in disease. uHTS can be a useful tool in investigating these orphan targets. Large collections of small molecules, natural products or peptides can be screened against these receptors after they have been cloned and expressed in test cell lines. Receptor agonists, identified from these screens can be used to explore the function of these receptors and to develop receptor antagonists. In this way, screening can be used, not only in the drug discovery phase, but also in the phase of target discovery. The benefit of uHTS at this point is to keep the cost low, where the likelihood that the target being studied has a high chance of not being useful.

The development of predictive tools for ADME and toxicity has become important to the development of new combinatorial libraries. Computational models can be used to guide the development of libraries with desired properties. To develop these models, one needs chemical and structural information from a set of representative molecules. This information can be obtained by screening large collections of molecules with *in vitro* assays for specific ADME or toxicity properties. Large and diverse libraries of molecules offer a rich source of information for the development of these predicative models. Screening these collections in uHTS format provides a powerful way to develop this information for model building.

These are just two benefits of uHTS technology beyond the original intent of speeding up the traditional targets-to-lead paradigm. The tools described in the Wölcke and Ullmann article will enable researchers to more effectively pursue and realize these benefits. As this new technology works its way into the laboratories of discovery researchers, I am sure we will see that it will change the way drug discovery is pursued in the future.

Reference

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