

As You Sow, So Shall You Reap: The European Gene Vector Production Network

Fintan R. Steele

Editor, *Molecular Therapy*

In one of the best-known but most widely misinterpreted parables of the Bible, the Kingdom of God is compared to a farmer who throws seed randomly about, hoping that some of it may fall on good ground. In 1997, the Association Française contre les Myopathies (AFM) provided funding for the Gene Vector Production Network (GVPN) under the direction of Généthon III in Evry, France. By making various gene transfer vectors and cell lines freely available to researchers in France, throughout Europe, and beyond, AFM hoped to spark increased interest in gene transfer that could lead, ultimately, to successful clinical applications for neuromuscular and other diseases. Four years later, the first full GVPN meeting was held in Evry on October 4 and 5 to determine how well these first seeds were sown and to plan future plantings. Several hundred users and associates of the GVPN presented research using GVPN-supplied vectors and discussed ways to further enhance this unique tool. It is clear to me that the GVPN has correctly interpreted the ancient parable for modern times.

The meeting presentations, poster and oral, covered a wide range of vectors (viral and nonviral) and investigations. Non-research presentations by the directors of the different GVPN centers showcased the physical facilities and specific abilities of the centers (currently in Evry, Nantes, and Marseilles, with a site in Barcelona possibly being added in the near future). The facilities described are all state-of-the-art and have varying capacities and specialties. Most of the research presentations focused on specific disease models (for example, protoporphyrrias and immunodeficiencies, in addition to neuromuscular disease). However, a sizable proportion also described the use of gene transfer technology to dissect out specific mechanisms of newly discovered genes and gene products. The common theme throughout was the use of GVPN-supplied vectors.

In his opening remarks, GVPN coordinator Mauro Mezzina pointed out that requests for GVPN vectors rose from 120 in 1997 to 631 so far in 2001. Although this may not seem like a large number, the lack of formal publicity for this service underlines the remarkable growth of this unique undertaking. In addition, requests are beginning to come in from around the world. However, as Mezzina noted, the value of the activity cannot be measured in numbers but rather must be evaluated in terms of the progress of science. To that end, it

seems that the GVPN has already provided a significant service in its short life.

Nevertheless, there are some major problems that have to be addressed. Mezzina and others noted that the network needs to be enlarged to other European sites, in terms of both the production capabilities and the dissemination of the vectors. Furthermore, it is critical that GVPN develop some form of shared platform with industry and regulatory agencies if the ultimate goal of clinical applications is going to be met. As with all other endeavors in the nascent European Union (EU), there are specific national and international hurdles to be cleared, not all of them scientific.

GVPN also faces scientific obstacles that are not limited to European national interests in gene transfer. To my mind, the largest of these is the issue of standardization in vector measurement and application. Although having one center supply all batches of a specific vector provides some form of "standardization" (that is, it is possible to compare experimental results from studies that obtained vectors from the one center), it is still impossible to compare results with other studies using the same vector but from different sources. The critical need for standardization of vector production and use remains one of the major stumbling blocks to interpretation of new gene therapy/gene transfer studies in relation to other published reports. This will require a concerted effort by researchers, industry, and regulatory agencies. Initial work on an adenoviral standard here in the United States is a step in that direction, but there is obviously a long way to go.

Another issue that transcends Europe is the funding for this kind of endeavor. AFM is incredibly generous in its funding of the GVPN, but it relies in turn for its money largely on the annual Telethon and the French public's support. The continued growth of GVPN in providing vectors to the rest of Europe and beyond will not be cheap, and may not be supported as well as direct research into neuromuscular disorders (the primary interest of AFM). To that end, a presentation by Gwennaël Joliff-Botell on the plans of the European Commission (EC) for its next "Framework Program" (2002–2006) to provide research money was, to my interpretation, a bit sobering. On the positive side, she pointed out the commitment of the EC to developing a robust European Research Area, identifying a more limited number of scientific priorities that are of strategic importance to the

EU (biotechnology is a particular interest) and where current EU strengths can be enhanced. However, it seems that the amount of money set aside for entire Genomics and Biotech division for the five-year program (2 billion Euros) is unlikely to provide a significant share for such an open initiative as the GVPN. Thus, funding will become increasingly more difficult without significant national input by EU member countries. Whether this would lead to a fragmentation of the GVPN along national lines remains to be seen.

Despite the difficulties, the approach taken by AFM via Généthon III in setting up the GVPN is an incredibly positive and far-seeing approach. Interpreters of the parable of the sower and the seed have often focused only on the seed that fell on good ground, and considered the other seeds somehow mistaken, wasted, or even wrong. However, the point of the parable is not the need to conserve seed, but rather the remarkable generosity of the

sower, and the fact that this apparent wastefulness is repaid many-fold. There is no way to know ahead of time where the successful seed will land: The widest possible spread ensures that some of the outcome will more than justify the profligate spreading. Although the reality is that precious resources should not be wasted, the willingness of AFM through GVPN to take substantial chances on a variety of research areas is a refreshing counterpoint to the limited and narrow focus of current governmental support, both in Europe and elsewhere. It also seems, from the initial analysis at the GVPN meeting, to be working. It should be hoped that as the GVPN grows it can marshal the resources necessary to maintain the openness that characterizes its current approach to supporting the spectrum of gene transfer research.

For general information about GVPN, or to apply for vectors, see <http://www.genethon.fr/gvpn/>.