PERSPECTIVE

The role of open innovation in biomarker discovery

Lilla Landeck[1*], Monika Lessl[2], Andreas Busch[2], Matthias Gottwald[2] and Khusru Asadullah[3]

[1] Department of Dermatology, Ernst von Bergmann General Hospital, Charlottenstrasse 72, 14467 Potsdam, Germany
[2] Bayer Global Drug Discovery, Müllerstrasse 178, 13353 Berlin, Germany
[3] Charité, University Medicine Berlin, Charitéplatz 1, 10117 Berlin, Germany

Abstract: Precision medicine aims to treat diseases with special consideration for the individual biological variability. Novel biomarkers (BM) are needed to predict therapeutic responses and to allow for the selection of suitable patients for treatment with certain drugs. However, the identification and validation of appropriate BMs is challenging. Close collaboration between different partners seems to be a key success factor. While the importance of partnerships and larger, well-established consortia in BM discovery such as the pharmaceutical industry and academic institutions is well understood and has been investigated in the past, the use of open-innovation models, also known as 'crowd sourcing for biomarkers', is still in its infancy. Crowd sourcing comprises of a — usually via internet — request for problem solution to an open group of users in a kind of an 'open call'. The community (crowd) is asked to provide solutions. Since the application of the crowd sourcing method offers the possibility to collect as many as possible novel ideas from a broad community with different expertise, this approach is particularly promising for BM development. In this article we describe the first examples of open-innovation models, such as the 'grants for targets' (G4T) and biomarkers initiative 'InnoCentive' (innovation/incentive) platform. They may be a fruitful basis for collaborative BM development in the future.

Keywords: open innovation, biomarker, precision medicine, crowd sourcing

*Correspondence to: Lilla Landeck, Department of Dermatology, Ernst von Bergmann General Hospital, Charlottenstrasse 72, 14467 Potsdam, Germany; Email: llandeck@klinikumevb.de

Received: August 28, 2016; **Accepted:** September 18, 2016; **Published Online:** October 31, 2016

Citation: Landeck L, Lessl M, Busch A, *et al*. 2016, The role of open innovation in biomarker discovery. *Advances in Precision Medicine*, vol.1(2): 1–4. http://dx.doi.org/10.18063/APM.2016.02.007.

Introduction

Lack or inadequate therapeutic effects are major reasons for failures in drug discovery. The use of 'biomarker (BM) stratified approaches', meaning that drugs are developed for particular and susceptible patient subgroups only, is expected to increase the number of medical approvals of such drugs. BMs may be effective tools to reduce attrition rates. Consequently, pharmaceutical companies started to invest significant efforts and money into BM stratified approaches. Besides the use of BM for patient stratification by predicting prognosis, therapeutic and adverse events, they may serve as surrogate markers for clinical endpoints. The overall goal of BM application in the clinical setting should be to increase drug efficacy leading to above-average success rates in the clinical treatment. Since BMs are of increasing importance in medicine and drug discovery, a higher need for identification and validation of suitable BMs can be expected[1–4]. This however, may be challenging. The reasons are manifold: physiological/pathophysiological and biological aspects have to be considered, and different technological aspects as well regulatory requirements have to be included. Therefore, complementary expertise and skills are required which may not be present in a single institution. In addition, the development of the BM may significantly

increase the total research and development costs, and sharing these costs by different partners may decrease the overall risk if a drug fails. Collaborations between academia, diagnostic and the pharmaceutical industry, best in consortia seem to be essential for successful biomarker discovery, development, and implementation. Indeed, collaborations between academic institutions and the diagnostics and pharmaceutical industry are increasingly being executed. These type of collaborations may help to improve research and development productivity in industry, as well as enable academic institutions to better exploit the translational potential of their research[5–9].

Along with the well-regulated collaborations between big partners, such as the pharmaceutical industry and academic institutions which were reviewed previously[6,7], the cooperation with young academic groups and biotech companies may be a fruitful basis for the development of innovative technologies and novel BMs[10]. Initiation of such collaborations may be difficult, in particular when the experience of the smaller partners in the interaction with big pharma companies is limited. For the 'big pharma' in turn, it may be hard to find appropriate smaller partners.

To encourage and support those potential smaller cooperation partners in participating in a problem solution, the method of *crowd sourcing* was developed and first introduced by Jeff Howe[11]. The initial application was in the Business to Consumer sector. In the original meaning, crowd sourcing comprised of a — usually via internet — request for problem solution to an open group of users in a kind of an 'open call'. The community (the crowd) is asked to provide solutions and the winning idea is rewarded.

Successful examples of this method such as the Procter & Gamble 'Connect and develop' portal (www.pgconnectdevelop.com) allows consumers to bring their ideas for product improvements or novel product ideas. According to Procter & Gamble, more than 50% of their product initiatives involve significant collaboration with outside innovators. Now, pharma companies are piloting this approach in drug discovery currently with a prime focus on new molecular targets. However, open innovation may also be useful for other areas such as new application systems, digital solutions and value-based healthcare.

Two pioneering approaches adopting the *'crowd sourcing'* scheme have been launched for biomarkers so far, including the *'InnoCentive platform'* and the *'Grants for targets and biomarkers initiative'*. These two open innovation initiatives are highlighted in the following article.

Crowd Sourcing in Drug Discovery

The first company to introduce this concept in drug discovery was Eli Lilly with the establishment of the InnoCentive platform (www.innocentive.com). Organisations in need of answers ('seekers') post specific questions ('challenges') on an internet marketplace. The web community ('solvers') can then provide solutions to the challenge. For each challenge, the seeking company can select the 'best' solution and the winning solver transfers the IP to the seeker and gets in return a financial reward. InnoCentive is now an independent organisation with a solver community of more than 200,000 experts in approximately 20 countries. Beyond drug discovery companies, other organisations such as SAP, Procter & Gamble, and the Rockefeller Foundation use the platform to find innovative solutions to their needs. Further crowd sourcing initiatives have followed in the past two years. In contrast to the 'classical crowd sourcing' concept, where the question is completed when an appropriate solution has been provided, the goal of business driven initiatives is to collect as many novel ideas as possible to be further pursued in a more collaborative approach[5].

The Use of the InnoCentive (innovation/incentive) Platform for Biomarker Discovery

The *InnoCentive* platform was established in 2001[5] (www.innocentive.com). It has a broad scope and is also comprised of BM challenges. For example, in 2015, a seeker asked for a specific and sensitive BM that is highly associated with liver fibrosis and could be used as a surrogate for clinical efficacy and ideally guide treatment selection. Another BM challenge was set up in 2008 to find a BM for disease activity of amyotrophic lateral sclerosis. This challenge attracted more than 1,000 teams who reviewed the prize criteria, and a total of 12 submissions were received from seven different countries. The prize was awarded to two 'solvers', who came up with preliminary BMs. However, more data are needed to validate their results (www.ideaconnection.com). Due to limited public information, it is not possible to give a final assessment on the overall success of the platform with regard to BM challenges yet.

The Grants for Targets and Biomarkers Initiative

Another example for an open innovation approach in

the BM field is Bayer's ' Grants4targets' (G4T) initiative (www.grants4targets.com), which was established in 2009 as a new approach for academic institutions to apply for grant support to pursue ideas on novel drug targets. In 2011, it was expanded to include BMs. The process, summarized in Figure 1, is as follows: after a review process, grants are provided to perform focused experiments for further validation of the proposed targets and biomarkers. In addition to financial support, Bayer provides specific know-how about target validation and drug discovery. Experienced scientists are nominated as project partners and, depending on the projects, tools or specific models are provided. By December 2015, more than 1,000 applications have been received, and 126 were for BMs (i.e., 15.5% of all applications). Eighteen BM projects have had approved grants, focusing on BM identification and/or BM candidate generation in cardiological, oncological and gynaecological indications, most often by applying novel technologies[12–14]. Since the G4T program is quite young, it is too early to judge its ultimate success for the identification and validation of BM. The first results, however, are very promising.

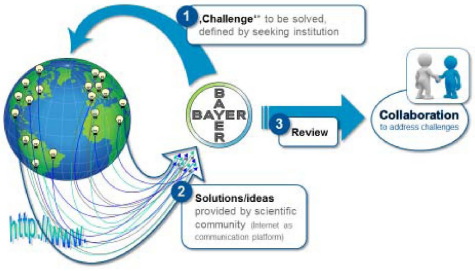

Figure 1. Crowd sourcing as partnering model to tap into the expertise of a large scientific community. The challenge can be the search for novel targets, biomarkers, compounds or indications for known assets. Adapted from Lessl *et al*., 2011, *Nature Reviews Drug Discovery*, 10, 241–242[5].

Summary and Conclusion

Open Innovation has been defined by H. Chesbrough[14] as the use of external and internal ideas and paths to create value. It has increasingly become popular and penetrated pioneering industries such as software, electronics or consumer industries[15]. Moreover, in the pharmaceutical industry, open innovation approaches are gaining in importance due to the pressing need to overcome the innovation gap. For the initial exploration of a new biomarker candidate or a novel technology, an open innovation approach seems to be suitable.

Crowd sourcing approaches, as described in this article, are an adequate approach to leverage the know-how of a large group of experts. To make it successful, key factors for open innovation approaches in drug discovery have to be taken into account (Table 1). It has to be carefully evaluated, whether the approach fits the challenge to be solved. Furthermore, an adequate budget is needed to fund the external activities, which might become challenging in economically difficult times. Also, internal resources to manage, support and complement external activities are required as well as an open mindset to ensure uptake of external ideas. Based on our experiences and the feedback we received from grant recipients, key prerequisites for success in the BM area are a fast and efficient processing of the requests, a low bureaucratic burden to generate and grant the proposals, and a face-to-face contact to the supported scientists after grant approval. This is strengthened by the fact that the know-how on drug development in academia is often limited and an intensive exchange is required to generate awareness and understanding for the entire process. Permeable boundaries and transparency in communication of

Table 1. Key success factors for crowd sourcing initiatives in drug discovery

Category	Factors involved
Strategic aspects	Evaluate suitability of crowd sourcing approach
	Define clearly what you are looking for and what you can offer to the community
Operational aspects	Create awareness for initiative, e.g., advertisements in key journals and direct mailings to scientific societies or key leaders in the field, presentation at conferences
	Communicate the submission and evaluation processes in a transparent manner
	Submit ideas quickly and with confidence for technical processes
	Ensure a transparent IP policy
	Keep bureaucratic hurdles low
Enthusiasm and Commitment	Prepare organisation for take up of external ideas
	Generate enthusiasm and commitment on all levels
Relationship Management	Generate trust by open and continuous communication
	Establish trustful relationship with Principal Investigators

Modified according to Lessl *et al*.: Crowd sourcing in drug discovery. *Nature Reviews Drug Discoveries*, 10, 241–242 (2011)[5].

needs and strategic interests are essential prerequisites to enable open innovation. However, these approaches are successful only if they are part of an overall strategy on how to deal with external innovation[7]. Key Performance Indicators defined for each initiative will be helpful to evaluate performance. It has to be pointed out that crowd sourcing initiatives in drug discovery are still in their infancy. Whether they will have a substantial impact on the development of novel BMs has yet to be proven. The first experiences are quite encouraging. We found that this type of collaboration attracts academic groups, offers the chance to get access to new partners and provides a valuable tool.

Conflict of Interest and Funding

LL has no conflict of interest to declare. ML, AB, and MG are employees and shareholders of Bayer AG. KA is a shareholder of Bayer AG.

Acknowledgements

The authors thank Stefanie Schoepe and Heidrun Dorsch (both from Berlin, Germany) for their valuable contributions in the G4T program and Johnny Grace (San Francisco Bay, USA) for critical reading of the manuscript.

References

1. Landeck L, Kneip C, Reischl J, *et al.* 2016, Biomarkers and personalized medicine: current status and further perspectives with special focus on dermatology. *Experimental Dermatology*, vol.25(5): 333–339.
2. Scannell J W, Blanckley A, Boldon H, *et al.* 2012, Diagnosing the decline in pharmaceutical R&D efficiency. *Nature Reviews Drug Discovery*, vol.11: 191–200.
3. Arrowsmith J, 2011, Phase II failures: 2008–2010. *Nature Reviews Drug Discovery*, vol.10: 328–329.
4. Salter H and Holland R, 2014, Biomarkers: refining diagnosis and expediting drug development — reality, aspiration and the role of open innovation. *Journal of Internal Medicine*, vol.276: 215–228.
5. Lessl M, Bryans J S, Richards D, *et al.* 2011, Crowd sourcing in drug discovery. *Nature Reviews Drug Discovery*, vol.10: 241–242.
6. Landeck L, Lessl M, Reischl J, *et al.* 2016, Collaboration for success: the value of strategic collaborations for precision medicine and biomarker discovery. *Advances in Precision Medicine*, vol.1(1): 25–33.
7. Asadullah K, Busch A, Gottwald G, *et al.* 2015, Industrial–academic collaborations for biomarkers. *Nature Reviews Drug Discovery*, vol.14: 805–806.
8. Wholley D, 2014, The biomarkers consortium. *Nature Reviews Drug Discovery*, vol.13(11): 791–792.
9. Stephenson D and Sauer J M, 2014, The predictive safety testing consortium and the coalition against major diseases. *Nature Reviews Drug Discovery*, vol.13(11): 793–794.
10. Lessl M and Douglas F, 2010, From technology-transfer to know-how interchange. *Wissenschaftsmanagement*, vol.2: 34–41.
11. Howe J, 2008, *Crowdsourcing: Why the Power of the Crowd is Driving the Future Business*. New York: Crown Publishing Group.
12. Lessl M, Schoepe S, Sommer A, *et al.* 2011, Grants4-targets — an innovative approach to translate ideas from basic research into novel drugs. *Drug Discovery Today*, vol.16(7–8): 288–292.
13. Dorsch H, Jurock AE, Schoepe S, *et al.* 2015, Grants4-Targets: an open innovation initiative to foster drug discovery collaborations between academia and the pharmaceutical industry. *Nature Reviews Drug Discovery*, vol.14*:* 74–76.
14. Chesbrough H, 2003, *Open Innovation: The New Imperative for Creating and Profiting from Technology*. Cambridge, MA: Harvard Business School Publishing.
15. Gassmann, O, Enkel E, Chesbrough H, 2010, The future of open innovation. *R&D Management*, vol.40(3): 213–221.