Real-life example of biobanking – results of the PATH Biobank

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Introduction

Since 2002, PATH Foundation has kept a biobank collecting high-quality fresh frozen breast cancer specimens adhering to uniform SOPs at seven certified breast cancer centres in Germany. According to informed consent, one sample is stored on trust for the patient. Remaining samples are donated for research purposes. Biobanking is organized in a decentralised manner. Breast cancer tissue, normal adjacent tissue and blood serum samples are stored at the institutes of pathology in vapour phase of liquid nitrogen. Annotating data sets are collected in PATH’s central data office in Munich. Research groups from academia and industry can obtain samples after application and review. PATH Biobank is a not-for-profit organisation and asks for a cost recovery fee in exchange for sample allocation to sustainably finance the expenses it incurs.

Methods

Decentralized biobank

- PATH’s samples are stored at 7 certified breast cancer centres in Germany (Figure 1)
- Tumour samples with ≥ 3 mm edge length
- Corresponding, normal adjacent tissue samples with ≥ 3 mm edge length
- All samples are stored in “fresh frozen” condition in the vapour phase of liquid nitrogen

Central database

- Data storage using Oracle® software and LIMS developed in-house
- Standardized forms for patients’ informed consent, approval by ethical review commission of the Uniklinik Bonn
- Central survey of patient-reported follow-up data

Results of the PATH Biobank

Since 2004, more than 8,000 breast cancer patients have given their informed consent to the storage and analysis of their tissue and blood serum for research purposes [1, Waldmann et al.]. Breast cancer tissue samples from 58% of donors could be stored due to the size of the surgically removed tissue specimen. In addition, normal adjacent tissue is available from 64% of donors and blood serum aliquots can be derived from 91% of patients. In total, a number of 7,132 tumour tissue samples (donated by 4,817 individuals), 7,083 normal, adjacent tissue samples and 15,257 blood serum samples could be stored in the biobank for research purposes (some of which is redundant storage). Figure 2 shows the total number of patients who have given their informed consent together with the distinct number of individual donors who respectively contributed to the different sample types.

Since 2008, all sample donors have been contacted individually to directly survey patient reported follow-up data. By now, information on the course of disease and therapy from 4,195 women has been collected. Median follow-up time is 38.5 months. If donors are lost to follow-up, missing follow-up data. By now, information on the course of disease and therapy from 4,195 women has been collected. Median follow-up time is 38.5 months. If donors are lost to follow-up, missing follow-up time is subject to the review process by an international scientific journal.

Conclusion

With its detailed clinical and follow-up data, PATH Biobank is a valuable, scientific resource for breast cancer research based on tissue and blood serum, e.g. biomarker studies. Since 2008, various research projects have successfully been conducted using PATH Biobank’s samples. Both, the quality and quantity of samples as well as the high quality of the data set made it possible to achieve the scientific purposes of these projects. Information on the studies using PATH’s samples and data is publicly accessible online [4, http://path-biobank.org].

Using PATH Biobank as a resource

Researchers from academic or industrial circles may apply for sample allocation by submitting a scientists’ proposal. Sample requests are reviewed by independent experts. PATH’s managing board decides on sample allocation advised by PATH’s board of trustees and scientific board. A material transfer agreement is signed, which also includes a cost recovery fee and reimbursement for logistics. For more information, please send an e-mail or visit: www.path-biobank.org

Disclosures

PATH Foundation has received donations from and/or has had sponsoring relations with the following companies: Aimgen, AstraZeneca, GlaxoSmithKline, MSD, Novartis, Pfizer, Pierre Fabre, Roche and vif.

Real-life example

PATH’s collaboration with Berlin-based Bayer Pharma AG, which started in 2012 and has been studying the frequency and background of defined mutations in breast cancer, is an outstanding example from real-life. [5, Rudolph et al.]. For this study the Bayer scientists designed a multi-step experimental setup in cooperation with PATH Biobank. Availability of defined tumour tissue samples, corresponding blood serum samples and follow-up data were essential preconditions for the feasibility of this project and were checked (in advance).

A number of 701 tissue samples were used for this study, comprising all seven sample source sites at PATH’s cooperation breast cancer centres. Local pathologists macroscopically assessed tumour content in PATH’s fresh frozen samples prior to biobanking. In addition, a central review of tumour content was planned as a first step of the analysis. For this purpose, one pathologist reviewed sections taken from the samples by microscopy. Results concerning tumour content of the samples are depicted in Figure 5, showing values related to sample-source sites (error bars indicate statistical mean and standard deviation).

Only 11% of tumour tissue samples failed due to lack of 5% tumour content. An overall number of 619 samples out of the 701 samples included complied with quality testing. Tumour content depended on clinical conditions and staging (ranging from 34% failure in samples derived from neoadjuvantly treated patients to 2% in cases when staging UCSC-Iv, for details see Figure 6).

In the next steps, shown in Figure 7, blood serum samples derived from the same individuals were analysed (point 2 in the flow chart). Furthermore, a subset of tumour tissue samples was sequenced on a next generation sequencing platform (point 3).

At the same time, the existing follow-up information was completed by querying local registry offices for survival data (this was done for the subsets analysed in steps 2 and 3 of the flow chart). Follow-up results are available for 96.3% of the cases with regard to overall survival. As different sources of information were used to gain follow-up data, details are shown in Figure 7.

Preliminary results of this study were presented at AACR 2014 [5, Rudolph et al.]. A detailed publication is subject to the review process by an international scientific journal.

Literature