

Disclosures

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

Introduction

Since 2002 PATH Foundation operates a biobank under uniform SOPs at seven certified breast cancer centers in Germany. High-quality fresh-frozen tissue samples are collected alongside with blood serum and FFPE specimen. 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.

In 2016 European scientists joined forces to form the MESI-STRAT consortium to address the unmet needs of women with ER-positive breast cancer supported by a Horizon2020 research grant. PATH Biobank is a co-coordinator within MESI-STRAT and will provide various samples to enable the research efforts.

Methods

Decentralized liquid nitrogen biobank

PATH's samples are stored at 7 certified breast cancer centres in Germany (Figure 1)

- tumor samples with ≥ 3 mm edge length
- Corresponding, normal adjacent tissue samples with ≥ 3 mm edge length
- Blood serum samples with ≥ 1 ml volume

All samples are stored "fresh frozen" in the vapour phase of liquid nitrogen

Dortmund
Bochum
Bonn
Kassel
Marburg
Offenbach



Figure 1: PATH's 7 sample source sites in Germany

Regensburg

Central database

Data storage using Oracle® software and LIMS developed in-house at central Munich based PATH Biobank office. A central patient reported follow-up survey is carried out every 24 months.

Ethics approval and informed consent

- Standardized and GDPR compliant informed consent of sample donors
- Ethical approval by the commissions of Uniklinikum Bonn and Bavarian Chamber of Physicians

Results of the PATH Biobank

Since 2004, more than 10,500 breast cancer patients have given their informed consent to the storage and analysis of their tissue and blood serum for research purposes [1]. Breast cancer tissue samples from 59% of donors could be stored due to the size of the surgically removed tissue specimen. In addition, normal adjacent tissue is available from 62% of donors and blood serum aliquots can be derived from 92% of patients. In total, a number of 8,382 tumor tissue samples (donated by 6,072 individuals), 9,401 normal, adjacent tissue samples and 10,021 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.

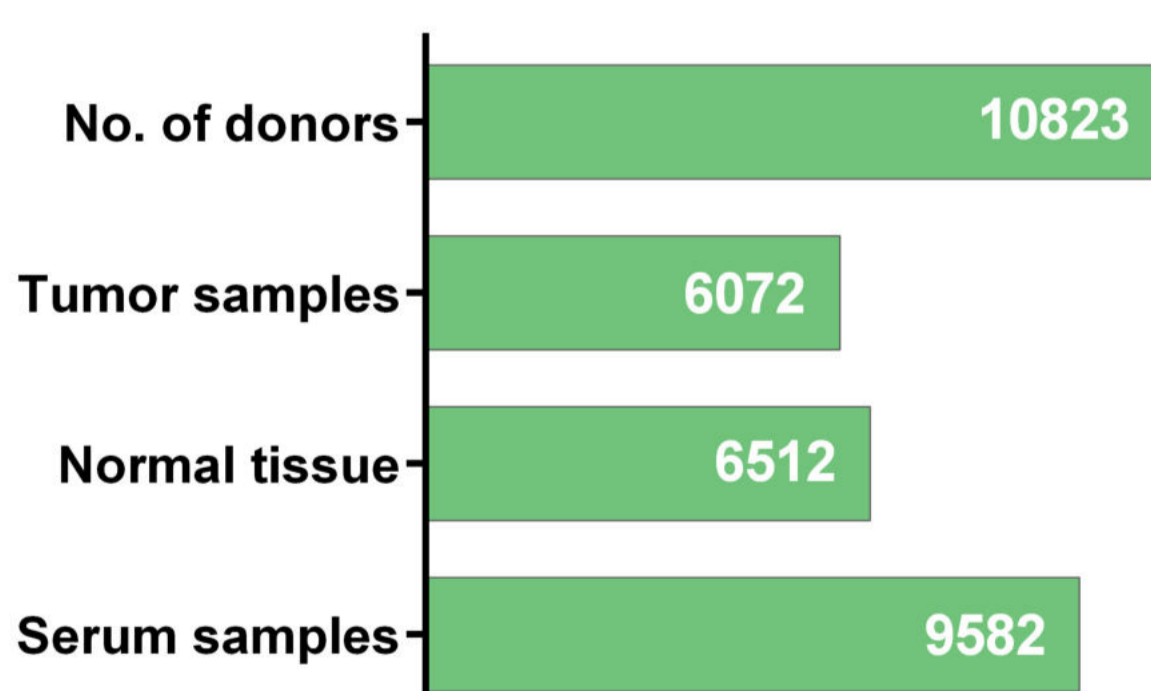


Figure 2: Numbers of donors and samples

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 7,864 women has been collected. Median follow-up time is 58.8 months. If donors are lost to follow-up, missing survival data can be inquired at registry offices.

By using the annotating data sets, it is possible to classify 96% of donors into the intrinsic molecular subtypes of breast cancer in accordance with the St. Gallen Criteria. For example, 66% of the cases belong to the Luminal A subgroup; the distribution of all PATH cases is shown in Figure 3. The UICC-stages are used as an alternative way to subgroup the patients (Figure 4).

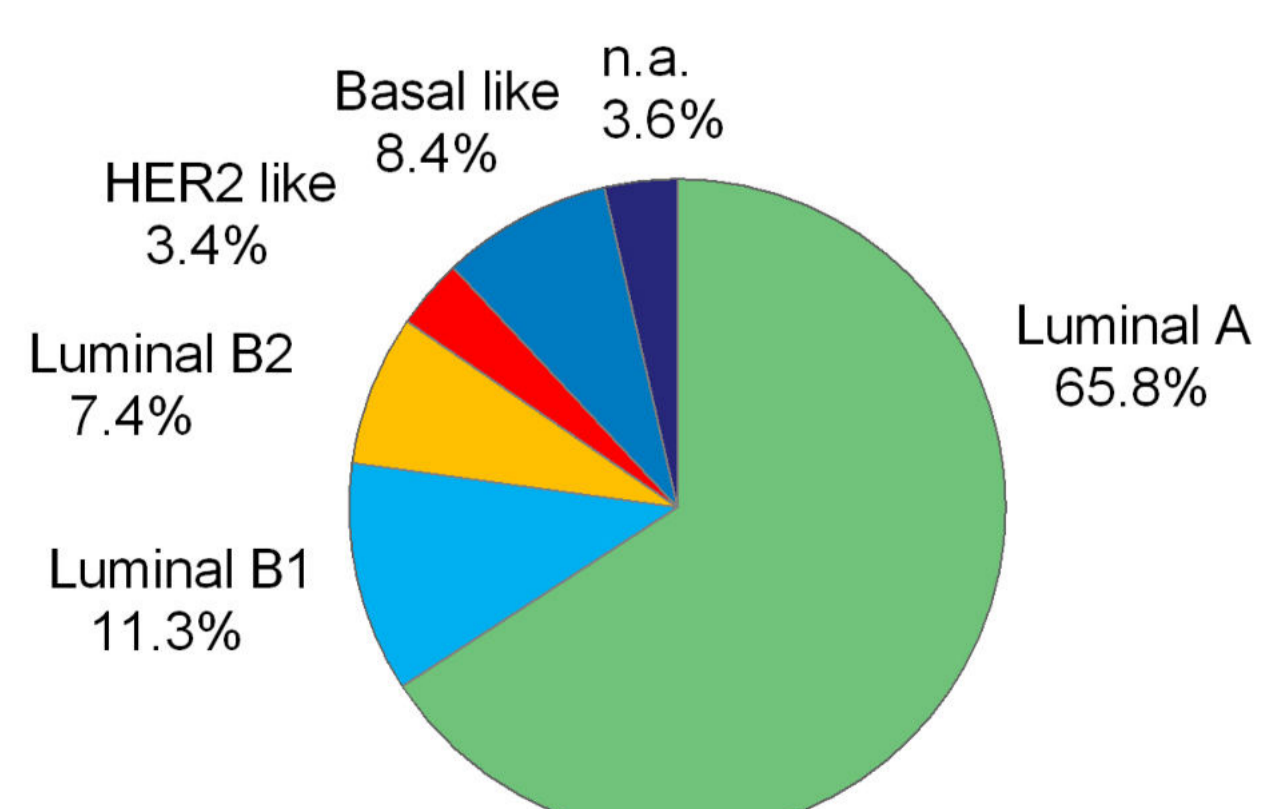


Figure 3: Distribution by intrinsic molecular subtypes*
* cases with neoadjuvant therapy, loco-regional recurrence or DCIS excluded

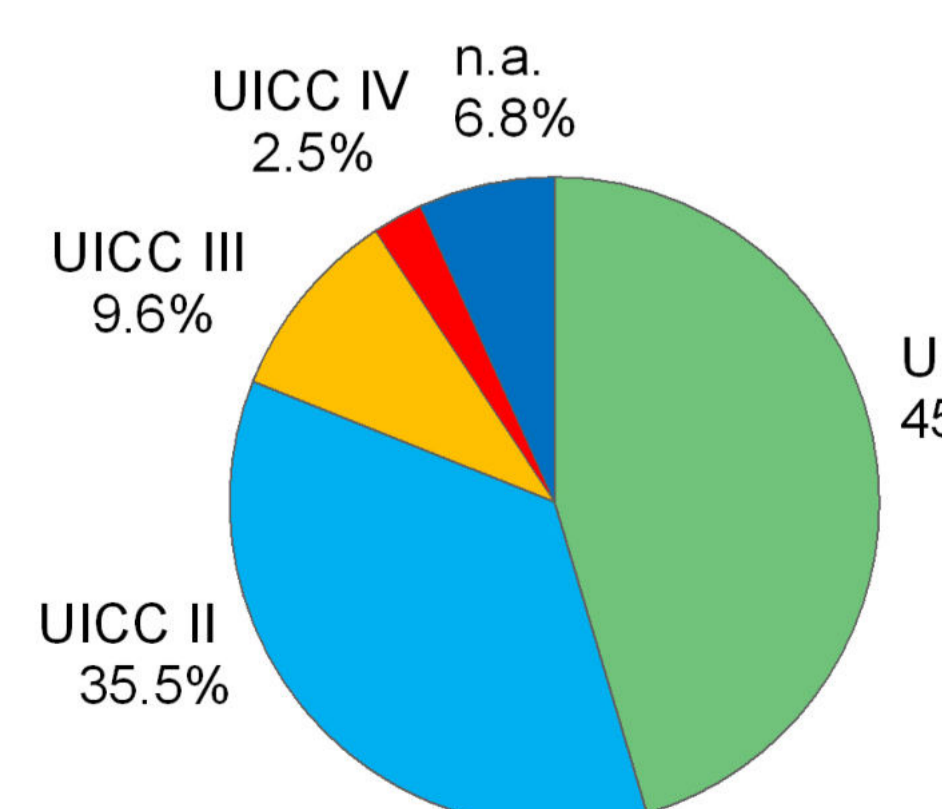


Figure 4: Distribution by UICC stages*

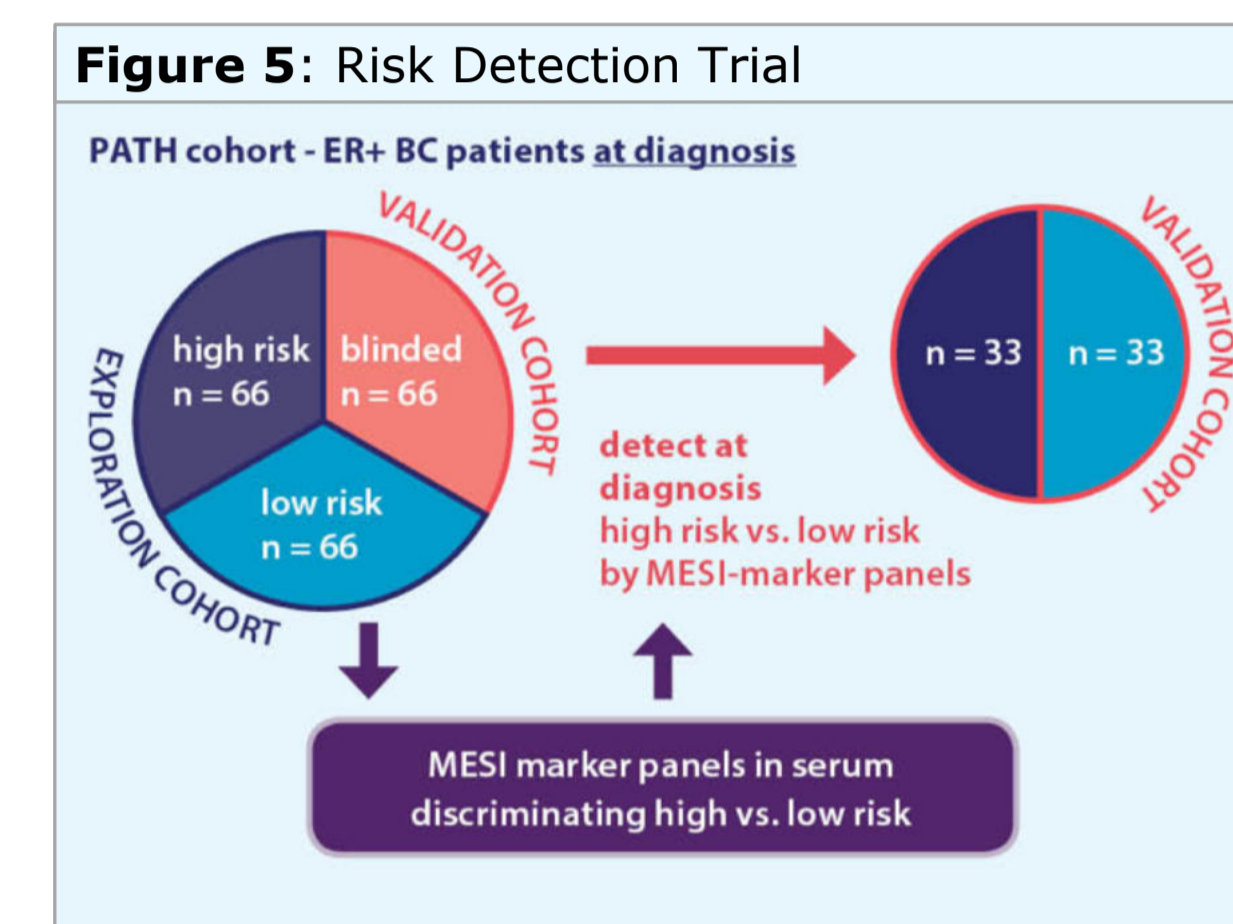
Contributing to EU-Horizon 2020 consortium MESI-STRAT

PATH Biobank joined the MESI-STRAT consortium, which is funded by a European Horizon 2020 research grant. MESI-STRAT will use systems medicine approaches to explore the interplay of breast cancer metabolism and oncogenic signaling in patients diagnosed with ER-positive disease.

The biosamples used for this research efforts will be provided within the framework of 10 clinical and preclinical studies. PATH Biobank has agreed to provide numerous samples donated by patients with a vast range of clinical subsets and outcomes.

Two studies will use blood serum and tumor tissue samples already archived in PATH Biobank, the details of this two studies are presented here.

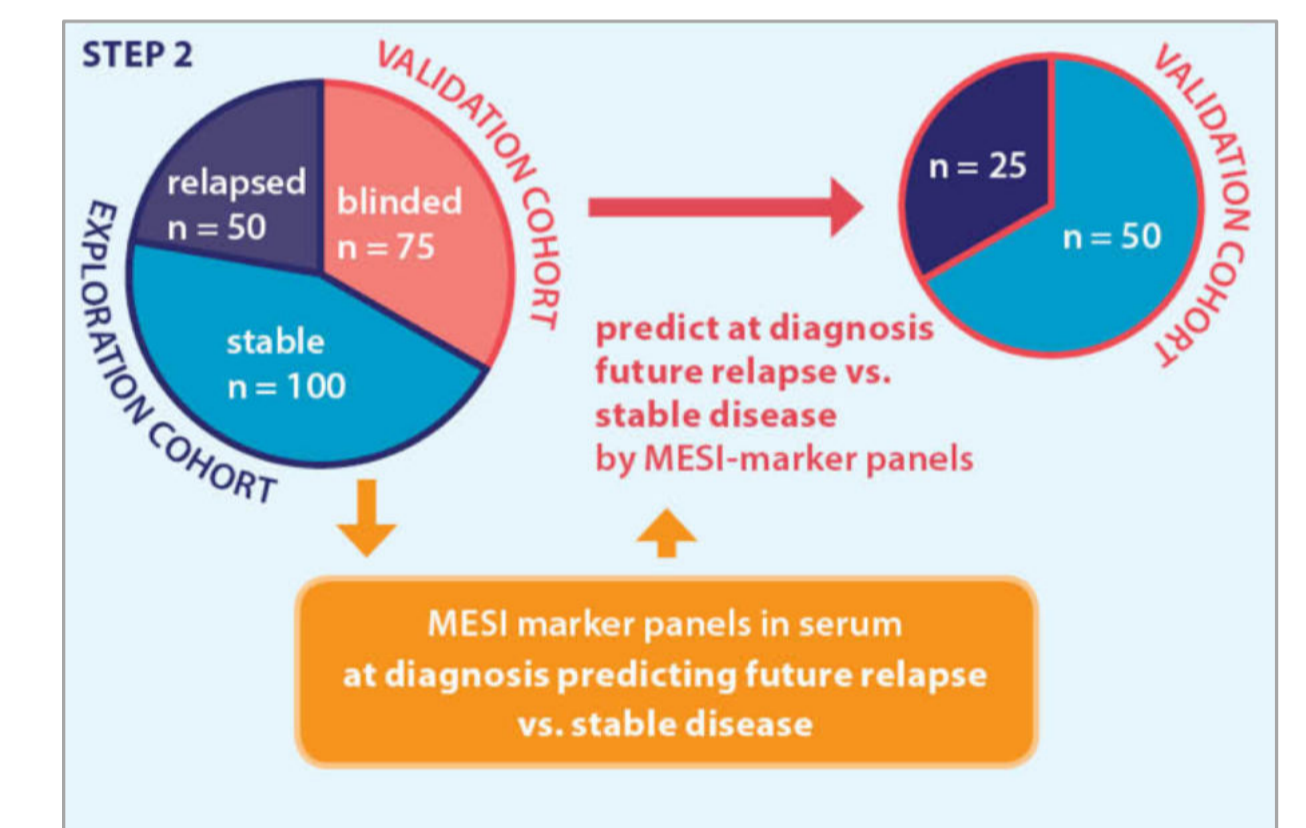
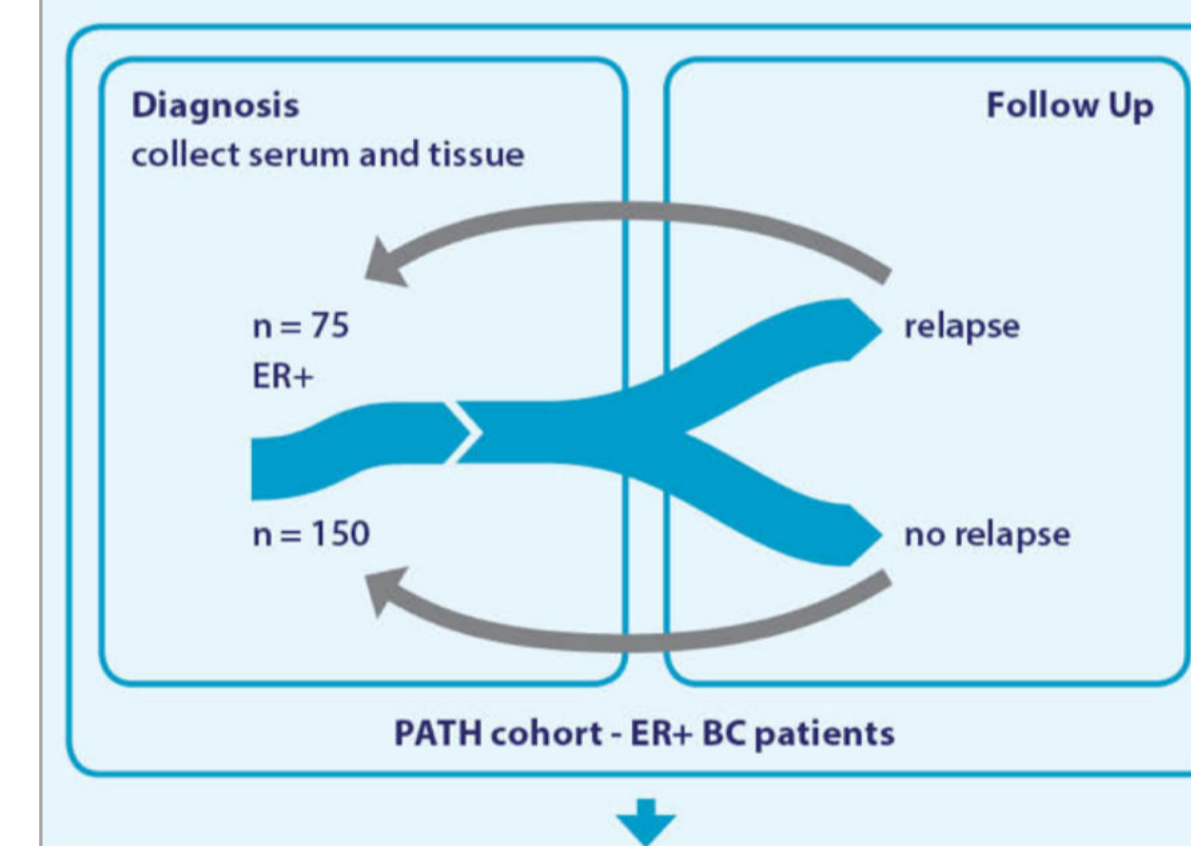
One study is called "Risk Detection Trial" and will use 200 blood serum samples, the other one is referred to as "Relapse Prediction Trial" and will be conducted using 225 blood serum samples. Within the "Risk Detection Trial" blood serum samples collected prior to breast cancer surgery from women with high and low risk ER+ disease will be used to identify signalling pathways and metabolites which allow detecting high and low risk patterns in blood samples of ER+ BC patients. Figure 5 shows details.



Blood serum samples allocated to the "Relapse Prediction Trial" were donated by ER+ patients prior to breast cancer surgery. Sample donors with extensive follow-up data regarding the course of disease are included. One group of patients developed distant metastasis after sample donation and during routine follow-up where as the second group of patients remained disease free regarding breast cancer for more than 5 years. Experiments using these biosamples aim to identify signalling pathways as well as metabolite biomarkers predictive for distant metastasis.

Figure 6: Relapse Prediction Trial

STEP 1 - selection of samples from patients with relapse versus stable disease during follow up



Furthermore, scientific investigations are performed on biosamples obtained from cell culture, PDX model and tissue bioreactor experiments. In addition, a longitudinal prospective collection of human biosamples will take place in two clinical programmes. One study is a "window of opportunity trial" conducted in Heidelberg/Germany in which antihormonal therapy is given in the neoadjuvant setting while within the "ET Termination Trial" organised by PATH Biobank biosamples are collected before and after the end of the regular, guideline-compliant antihormonal therapy.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 754688.



Conclusion

With its detailed clinical and follow-up data, PATH Biobank is a valuable, scientific resource for breast cancer research based on tissue (both fresh frozen and FFPE samples) and blood serum, e.g. biomarker studies. Since 2008, various research projects have successfully been conducted using PATH Biobank's samples [2, 3]. Both, the quality and diversity of samples as well as the integrity of annotating data sets, made it possible to achieve the scientific purposes of these projects. Research work and associated sample allocation are published on the website of PATH Biobank [4]. The purpose of PATH Biobank and its objectives will be further implemented by upcoming research efforts e.g. the Horizon2020 consortium MESI-STRAT.

Using PATH Biobank as a resource

Researchers from academic or industrial circles may apply for sample allocation by submitting a 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 info@stiftungpath.org

Literature

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