Supplementary information for *"TMA Navigator: network inference, patient stratification and survival analysis with tissue microarray data"*

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Supplementary Figure S1: TMA Navigator workflow. The figure has embedded hyperlinks which open to relevant sections of the user guide on the website. The first step in using TMA Navigator is to upload a table of marker scores. Following successful validation, data are annotated with a title and (optionally) notes. Options for score type (categorical or continuous), aggregation of replicates and batch correction are selected, as applicable. Data import with the selected options is initialised and the dataset added to the queue. Once processed, the dataset is ready for analysis from the 'dataset page'. At this stage, survival data may optionally be "attached" to the dataset by uploading a separate file. Analyses can be run from a dialog box accessed from the 'dataset page', and output is provided in a 'completed results' table. Datasets and results can be revisited using a unique key-protected URL (anonymous users) or by logging in (registered users).

Marker heatmap on Breast Cancer 1 (AQUA)

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Supplementary Figure S2: Marker heatmap. Pairwise Spearman correlation is visualised as a heatmap (left) on a blue-grey-orange scale (right). The order of markers is determined by hierarchical clustering using complete linkage (far left and top-left). The main diagonal indicates self-correlation, always 1 by definition. The highest correlation cluster contains E-cadherin and β-catenin, which form an adhesion complex important in maintaining epithelial state. Snail, ZEB2 and Vimentin form another cluster; Snail and ZEB2 are EMT transcription factors which can both induce Vimentin expression, a known mesenchymal marker.

Kaplan-Meier (tertile) plots on Breast Cancer 3 (IHC Quickscore)

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PTEN pAKT.nuclei pAKT.cyto HER2



Supplementary Figure S3: Stratification of trastuzumab treated breast cancers by tertiles of PTEN expression. Kaplan-Meier plot: x-axis denotes overall survival in months, y-axis the proportion of the group alive. PTEN has previously been shown to have a role in resistance to trastuzumab, and a significant positive relationship with survival was identified (FDR p=0.0207). The numbers of patients in each group is not identical due to the semi-continuous scoring system, where multiple patients take the same value at the group boundary.



IIII TMA Navigator

Supplementary Figure S4: TMA Navigator architecture. The figure has embedded hyperlinks which open to the homepage of the relevant software, where applicable. TMA Navigator is a web application comprising several server-based software components. Users connect to the service using a web browser, which accesses web pages on an Apache web server. The site is written in Python using the Django web framework. Data are stored on the server file system and in a PostgreSQL database. Submitted 'jobs' – importing data, running analyses – are computed asynchronously using a RabbitMQ message queue system. When sufficient computing resources are available, a Celery worker node retrieves the next available job from the queue, if any, and executes it using a custom software library written in the R language. The results are saved to the file system and database for subsequent retrieval by the web server upon user request.

Target	Source	Catalogue No.	Host
E-cadherin	BD	610181	Mouse
Claudin7	Abcam	ab75347	Rabbit
N-cadherin	BD	610921	Mouse
Vimentin	Sigma	V 6630	Mouse
Fibronectin	Abcam	ab2413	Rabbit
Zeb2	Acris	ZFHX1B	Rabbit
Zeb1	Gift from D. Darling	n/a	Rabbit
Slug	LifeSpan Bio	LS-C30318	Rabbit
Snail	Abcam	ab17732	Rabbit
β-catenin	BD	610153	Mouse
MAL2	Abcam	ab75347	Rabbit
C35	Vaccinex	(VX35)	Rabbit
Her2	Dako	A0485	Rabbit
ER-alpha	Vector	VP-E613	Mouse
ALDH	BD	611194	Mouse
PTEN	Cell Signaling Technology	9552	Rabbit
рАКТ	Cell Signaling Technology	4060	Rabbit

Supplementary Table S1: List of antibodies used for AQUA immunofluorescence. Sodium citrate pH 6.0 was used for antigen retrieval.