Purpose:

To provide researchers with a tissue microarray of formalin fixed paraffin embedded samples pancreatic invasive carcinoma and intraepithelial neoplasia (PanIN), including high and low-grade pancreatic PanIN and nodal and distant metastases collected from the patients whose primary invasive tumor is also represented. Also included are benign ducts from both benign and malignant pancreas samples. This TMA may detect strong trends in differential gene expression among different stages of pancreatic cancer progression; it is intended for pilot surveys and generation of hypotheses. This TMA is not designed to prove the utility of a marker for clinical prognosis.

Tissue samples:

The following tissue types are represented in the original TMA design:

- 14 cases of invasive pancreatic adenocarcinoma (conventional type)
- 8 cases of low-grade PanIN, including 4 from benign and 4 from malignant cases
- 7 cases of high-grade PanIN, all from malignant cases
- 7 cases of non-nodal pancreatic adenocarcinoma metastases
- 10 cases of lymph nodal pancreatic adenocarcinoma metastases
- 5 cases of normal pancreatic ducts from malignant cases
- 4 cases of normal pancreatic ducts from benign cases

Notes:

1) There is considerable, deliberate overlap in the patients represented on this array. This is to facilitate investigation for changes in gene/biomarker expression across the progression of an individual neoplasm: for instance, the array includes several examples of low-grade PanIN, high-grade PanIN, primary tumor, and metastatic tumor all from the same patient. These are designated as "redundant patients" in the Grid Code.
2) Non-nodal distant metastases derive from liver (4 cases), lung (1 case) and omentum (2 cases). Metastatic sites are designated in the Grid Code.

TMA design:

Each case is represented in a single 1.5 mm core in the original array design. There are four duplicate PancProg1 blocks slated for dispersal, designated A, B, C and D. Each array block is serially sectioned at 4 micron thickness. The histologic sections are placed on charged glass slides (Superfrost Plus, Fisher Scientific). At intervals, sections are stained and examined by a pathologist for quality assurance (QA) purposes.

The TMA also contains control tissues that provide orientation for the TMA slide:

Kidney
Placenta

Quality assurance procedures:

Due to the variability inherent to tissue samples and histologic methodology, *most of the tissue microarray sections will not contain all of the tissue spots in the original design.* The number of tissue spots in which the desired tissue types resides will vary from section to section.

The following guidelines are used during histologic quality assessment:
A tissue spot is defined as being present if tissue occupied at least 25% of the possible surface area OR if at least 10 cells of target tissue are present. Target tissue is defined as being present if at least 10 cells were present in a tissue spot. TMA slides are being released up to the histologic level in which there at least 10 cases present for primary invasive carcinoma and at least 5 cases present for low-grade PanIN, high-grade PanIN, nodal metastases, non-nodal metastases, and normal ducts (including both cancer and non-cancer cases). Thus at a minimum, there will be 35 tissue samples on the TMA section, representing the full range of pancreatic neoplastic progression. Copies of the QA scoring sheets are also available upon request.

THE TISSUE SAMPLES HAVE BEEN ANONYMIZED, NO FURTHER DATA ON THE DONORS IS AVAILABLE OTHER THAN THAT FOUND IN THE ACCOMPANYING GUIDE SHEETS.

Guide sheets in Microsoft Excel format and H&E stained whole-slide images representative of the array are available on the CHTN TMA website: http://chtn.sites.virginia.edu/.

If despite our efforts there are fewer than the minimum number of target tissue samples on your array sections, please contact the CHTN Mid-Atlantic Division at (434) 924-9879.

Frequently asked questions:

Why aren't all there as many tissue spots on my section of the array as are listed on the TMA key?

> The key represents the original TMA design. Tissue cores are of various lengths, hence at deeper sections, some cores have been exhausted while others remain. In addition, some tissue spots may be lost during the process of transferring the TMA section to the glass slide.

Why isn't the target tissue type present in the tissue spot?

> Although TMA manufacture is guided by a histologic section that represents the surface of the donor tissue, this target tissue may not be uniformly represented in the deeper sections of the tissue. This problem is greatest with small structures (e.g. breast ducts and lobules).

Why doesn't the representative microscopic image of the target tissue exactly match the tissue spot on my TMA?

> The representative images have been taken from a single spot from a single QA section from a single array. Four different replicate TMA blocks were made for this series, each of which has different tissue cores. Even the same tissue core at a deeper section would not exactly match a more superficial section due to the variability inherent in tissue architecture.

Can I use antigen retrieval methods (boiling, microwave, pressure cooker, etc) on these sections?

> Yes.

Can I perform in situ hybridization on these sections?

> Yes.

Definitions and abbreviations:

Donor block: a tissue paraffin block (see below) that contains tissue of the desired type to be placed into the tissue microarray.

Histologic section: a flat sheet of paraffin and embedded tissue cut from a paraffin block on a microtome. The thickness of the section can vary, but a typical thickness is 4 microns (micrometers).

QA: quality assurance

Recipient block: The blank paraffin block into which tissue cores are inserted to form the tissue microarray.

Tissue core: the cylindrical tissue sample removed from the donor block, which is placed in the recipient block.

TMA: tissue microarray. A recipient paraffin block into which tissue cores have been inserted in a gridded array.

Tissue paraffin block: a sample of tissue that has been fixed in formalin, processed to remove water, then infused with molten paraffin, which is allowed to harden within and around the tissue in a square mold. This is the standard method of preparing tissue for clinical histologic analysis. The paraffin block is subsequently cut on a microtome to produce thin histologic sections which are placed on glass slides. In the manufacture of TMAs, these become the donor blocks.

Tissue spot: the tissue sample present on a histologic section of a tissue microarray that corresponds to a tissue core.