A comprehensive information database (CID) of breast cancer patients in China

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Breast cancer is a leading cause of morbidity and mortality among female cancer patients in China and the world [1]. Although having yielded a great deal of knowledge in the last three decades, basic breast cancer research is often conducted using cultured cells that mimic tumors only to a certain extent. Likewise, the use of mouse models to investigate breast cancer has its obvious limitations. The combination of tumor samples and patients’ clinical information can facilitate the discovery of new biomarkers, which can be used to benefit new tumor patients. However, the acquisition and access to tumor specimens as well as comprehensive information on patients have been a bottleneck in breast cancer research. A comprehensive information database (CID) allows scientists to assess and verify the clinical relevance of basic findings, thereby providing an essential link between basic and applied research [2,3]. The recent advances in genomics, proteomics, biotechnology, and information technology led to the establishment of many national tumor bank networks, such as the Spanish National Tumor Bank Network (SNTBN), which aims to collect tumor banks across Spain.

A promising area in cancer research is the identification and characterization of biomarkers that can predict the response of cancer to treatment. CID has played pivotal roles in evaluating diagnostic tools and therapeutic reagents, including human epidermal growth factor receptor 2 (HER2)/Neu (amplified in some breast cancers), prostate specific antigen (PSA) test, and cancer antigen 125 (CA125) antigen test for ovarian cancers. The CID of the Department of Breast Pathology and Research of Tianjin Medical University was founded in 2003 with the aim of creating a bridge between basic research and clinical resources. Located in a major tumor hospital, the department collects comprehensive information from all patients (i.e., epidemiology, breast imaging, clinical findings, immunologic findings, susceptibility of tumor cells to abnormal breast tissue, etc.) and various tissue samples (i.e., peripheral blood, normal and abnormal breast tissues, etc.). CID has collected more than 10 000 cases and continues to provide support to many research projects across China [4,5]. This database will become a powerful tool in facilitating the development of clinical and translational medicine.

Necessity of establishing a breast tumor bank in China

Although the incidence of breast cancer is lower in China than in western countries, it is rising at a rapid pace [6]. According to Chinese government reports, female breast cancer deaths have climbed to nearly 40% in the last decade, and the disease is affecting a younger group — women between the ages of 45 and 49. Breast cancer morbidity in Chinese women starts to increase at age 20 to 25 and reaches its peak at age 45 to 50. These age ranges are ten years earlier than those of women in western countries.

The guidelines for breast cancer treatment in China mainly come from the National Comprehensive Cancer Network (NCCN), which was based on clinical practice in western patients. However, the NCCN guidelines may not be perfectly suitable for Chinese women because of the difference in the genetic background and lifestyle. The risk factors of breast cancer in China are also different. Chinese women ingest less fat and more soy food compared with western women. A high soy intake during adolescence may reduce the risk of breast cancer in later life [7], and a lower intake of fat may further reduce this risk. Accumulating epidemiological evidence suggests that sex steroid hormones are positively associated
with the development of breast cancer. The mean estradiol concentrations in British women in the 35 to 44, 45 to 54, and 55 to 64 age groups are 6%, 90%, and 171% higher than those in Chinese women, respectively [8]. Numerous studies have demonstrated the differences in breast cancer among women of different racial and ethnic groups [9]. Japanese and Chinese women present less advanced stages and have higher survival rates compared with non-Hispanic whites [10,11]. Asians are more likely to have ER-negative/PR-negative breast tumors than non-Hispanic whites [12]. The HER2+ subtype is more prevalent in the Chinese than in western populations [13]. Studies on breast cancer in Chinese women mainly focus on Chinese immigrants to the western world. However, these immigrants are likely to adopt a western-style diet and are not under the long standing one-child policy of China. All these factors may modify the risk of breast cancer. Therefore, a breast tumor database in China is necessary to facilitate the development of breast cancer treatment guidelines for Chinese patients. The CID on breast cancer patients will also facilitate the translation of basic research to clinical medicine, specifically for Chinese breast cancer patients.

**Department of Breast Pathology and Research**

The Department of Breast Pathology and Research is the only institution in China solely dedicated to breast cancer diagnosis and research. The department brings together state-of-the-art technology and highly trained personnel to provide a comprehensive diagnosis of breast cancer. The goal of our basic and translational research is to understand breast cancer processes and provide therapeutic guidance. Currently, the department has 29 staff members, consisting of 10 pathologists, 4 scientists, 4 postdoctoral fellows, 8 technicians, and 3 secretaries. More than 30 graduate students and 2 overseas students are under training for doctorate or master’s degrees in this department.

The Department of Breast Pathology and Research is structurally divided into four main diagnostic services: histopathology, molecular diagnostics, genetic diagnosis, and drug chemotherapy sensitivity test.

1. **Histopathology.** Total diagnosis: > 9,000 cases/year (> 2,800 breast cancer). Immunohistochemistry: > 8,000 cases/year. Frozen section diagnosis: > 3,000 cases/year. Pathology consultation: > 3,000 cases/year.

2. **Molecular diagnostics.** Fluorescence in situ hybridization (FISH): > 600 cases/year. Nipple discharge carcinoembryonic antigen (CEA) Test: > 100 cases/year. One-step nucleic acid amplification (OSNA): > 100 cases/year.

3. **Genetic diagnosis.** > 60 cases/year.

4. **Chemotherapy drug sensitivity test.** Collagen gel droplet embedded culture drug sensitivity test (CD-DST) > 2,000 cases/year.

**Tumor procurement protocol and CID establishment**

1. Ethics and consent process: A day before the surgery, patients willing to participate sign an informed consent form, indicating their approval of the use of the remaining tissue for research purposes after the histopathological diagnosis.

2. Basic information, such as age, nationality, menstrual status, methods of contraception, family history, breastfeeding, gestation/delivery, and so on, was collected by a nurse.

3. After surgical excision, the entire specimen was immediately transported to the Department of Breast Pathology and Research.

4. The staff recorded the time of surgery and the time at which the tissue was excised. All tissues were submitted for routine histology to ensure that no compromise of patient service is made. If excessive tumor tissue was available, it was collected by the staff from CID.

5. Part of the specimen was used for primary breast cancer cell separation and for the chemotherapy sensitivity test.

6. For each specimen, the following were available for research: (a) fresh tumor tissue; (b) formalin-fixed and paraffin-embedded (FFPE) block and slides; (c) fresh normal breast tissue; (d) fresh lymph node with metastatic carcinoma; (e) primary breast cancer cells; and (f) supernates of the primary breast cancer cell culture media. To maintain the protein and RNA quality, frozen tissues were first stored in liquid nitrogen and then placed in −80°C. The standard operation protocol for each step in tissue collection and processing were derived mainly from Snell et al. [14], with some modifications.

7. A comprehensive and dedicated database for each specimen consisting of the clinical information of the patients was maintained.

8. Follow-up information on the patients was obtained.

**Resources**

The facility space and equipment required for the CID are as follows:

1. Tissue processing room. Tumor tissues are delivered directly from the operating room to the tissue processing room, and a gross examination is conducted by pathologists.

2. Freezer space. Ultralow freezers and liquid nitrogen tanks provide sufficient space for the collection of breast tumor tissues.

3. Research laboratory. Majority of the molecular studies such as RNA/DNA/protein extraction, polymerase chain reaction (PCR), electrophoresis and visualization of PCR products, real-time PCR, Western blots, and immunohistochemistry are performed in this laboratory.

4. Slides and paraffin tissue storage room. More than