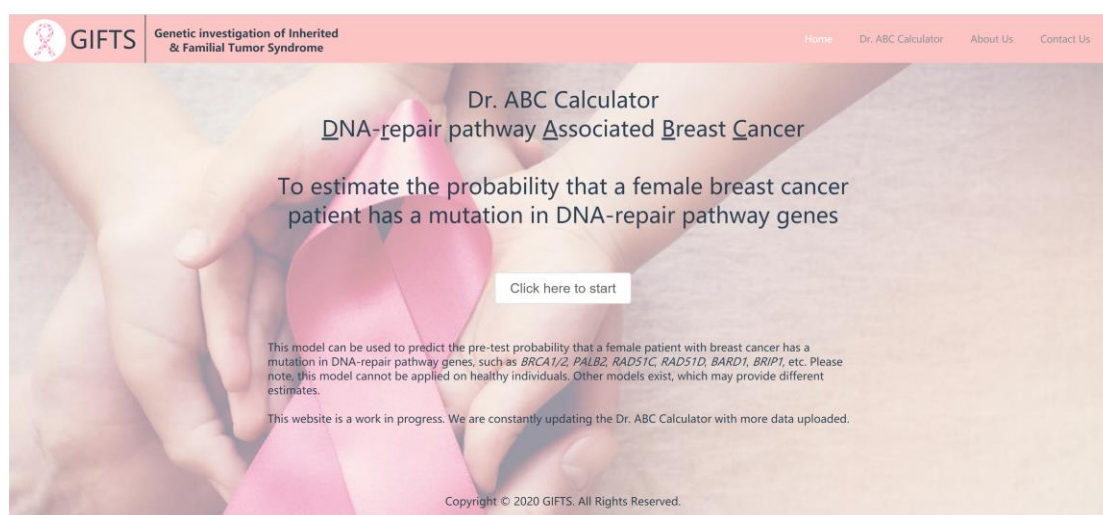


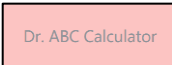
A user guide for the DrABC model

The DrABC (DNA-repair associated breast cancer) model was designed to calculate the risk of carrying a germline pathogenic variant in cancer predisposition genes for female patients with breast cancer. Currently, this model has only been trained and validated in the Chinese population, whose performance in other populations is still uncertain. The DrABC model was implemented in a website interface, which is easily accessible at <http://gifts.bio-data.cn/>. This online tool is available for healthcare providers and researchers. Please note this mode is not licensed to support clinical or diagnostic decisions.

Several steps to calculate the risk are described below.

1. Start calculation



Click the  or the  button to start to calculate the risk of carrying a germline pathogenic variant in cancer

predisposition genes for female patients with breast cancer.

2. Provide the clinical information of the proband

GIFTS Genetic investigation of Inherited & Familial Tumor Syndrome

Home Dr. ABC Calculator About Us Contact Us

Pathogenic mutation risk in DNA-repair pathway genes

Enter the clinical and pathological characteristics of a female breast cancer patient to calculate her risk to have a pathogenic mutation in DNA-repair pathway genes.

Personal & Clinical Information

* Age (e.g. 45)

Tumor size(cm) (e.g. 2.00)

* Histological Grade (e.g. High Grade(III))

* Estrogen receptor (ER) Grade (e.g. +++)

* HER2 (e.g. Negative)

* EGFR (e.g. +++)

* Multifocal (e.g. Unifocal)

* Bilateral (e.g. Unilateral Breast G.)

* E-mail

Cancer History & Family History

* Age at onset (e.g. 45)

ki67(%) (e.g. 30)

* Androgen receptor (AR) Grade (e.g. +++)

* Progesterone receptor (PR) Grade (e.g. +++)

* P53 (e.g. 1-70% wild-type)

* CK5&6 (e.g. +++)

* Lymph node status (e.g. Lymph node metas)

Next

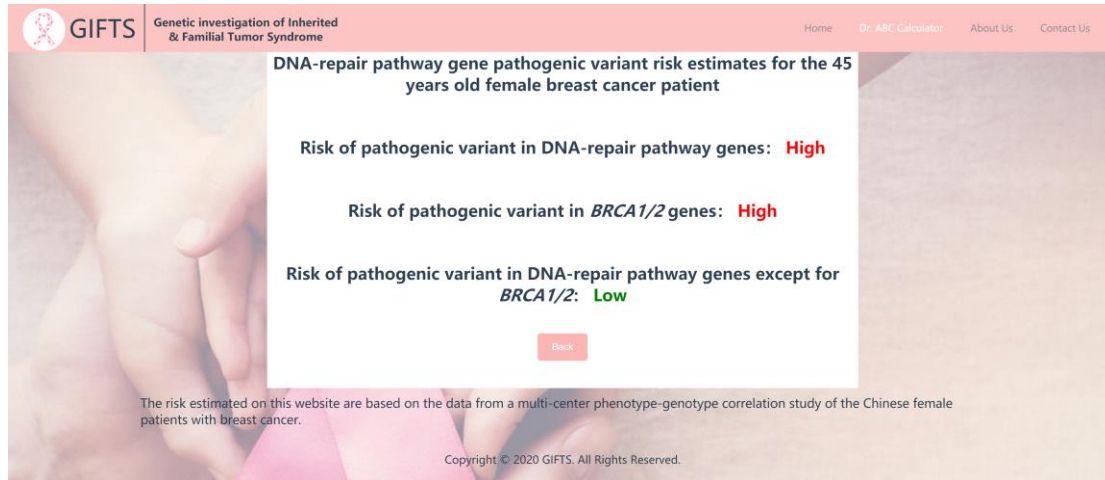
Information should be typed in the boxes as examples. Values with * are required, such as current age and the age at diagnosis. However, an “unknown” option was set for the pathological features. Thus, the missing data of the pathological features including Histological Grade, Androgen receptor (AR) Grade, Estrogen receptor (ER) Grade, Progesterone receptor (PR) Grade, HER2 status, P53 status, EGFR status, CK5&6, Bilateral or Unilateral, Multifocal or Unifocal, and Lymph node status, is tolerant. As numerical continuous variables and categorical variables are both present in our scenario, the missing data is imputed using proximity from random forest algorithm [Breiman L. Machine Learning 2001;45:5–32.]. An email of the researcher is also needed for further follow-up.

3. Provide the personal and family cancer history

The screenshot shows the 'GIFTS' web application interface. The header includes the logo and navigation links: Home, Dr. ABC Calculator, About Us, and Contact Us. The main heading is 'Pathogenic mutation risk in DNA-repair pathway genes'. Below this, a sub-heading reads: 'Enter the clinical and pathological characteristics of a female breast cancer patient to calculate her risk to have a pathogenic mutation in DNA-repair pathway genes.' The form is divided into two main sections: 'Personal & Clinical Information' and 'Cancer History & Family History'. The 'Cancer History' section on the left lists various cancer types with checkboxes: Ovarian, Thyroid, Lung, Colorectal, Lymphoma, Gastric, Brain, Endometrial, Teratoma, Cervical, and Renal. The 'Cancer History & Family History' section on the right is titled 'Patients count in 1st-3rd relatives' and lists cancer types with corresponding input fields: Breast cancer, Ovarian cancer, Pancreatic cancer, Esophageal cancer, Laryngeal cancer, Prostate cancer, and Male breast cancer. Each input field has a minus, zero, and plus button. At the bottom of the form are 'Back' and 'Submit' buttons. A disclaimer at the bottom states: 'The risk estimated on this website are based on the data from a multi-center phenotype-genotype correlation study of the Chinese female patients with breast cancer.'

The user could select the cancer type which the proband has suffered. The patient number of the responding cancer type in the 1st-3rd degree relatives is also required. For example, if a sister, mother, anti, great-grandmother, second-cousins, and great-great-grandmother of a proband all have the breast cancer, the patients count in 1st-3rd relatives is 4 as the second-cousins and great-great-grandmother are the 4th-degree relatives. The ages at diagnosis of other cancer types for the proband and ages at diagnosis for the relatives are not required, as this information is often not available in clinical practice.

4. Risk estimation



The screenshot displays the GIFTS (Genetic investigation of Inherited & Familial Tumor Syndrome) website. The header includes the GIFTS logo and navigation links: Home, Dr. ABC Calculator, About Us, and Contact Us. The main content area, titled "DNA-repair pathway gene pathogenic variant risk estimates for the 45 years old female breast cancer patient", shows three risk levels: "Risk of pathogenic variant in DNA-repair pathway genes: High", "Risk of pathogenic variant in *BRCA1/2* genes: High", and "Risk of pathogenic variant in DNA-repair pathway genes except for *BRCA1/2*: Low". A "Back" button is located below the risk estimates. A disclaimer at the bottom states: "The risk estimated on this website are based on the data from a multi-center phenotype-genotype correlation study of the Chinese female patients with breast cancer." The footer includes the copyright notice: "Copyright © 2020 GIFTS. All Rights Reserved."

As a result, the DNA-repair pathway gene pathogenic variant risk for the female breast cancer patient with the responding features was estimated. The risks of carrying germline pathogenic variants in *BRCA1/2* or other cancer predisposition genes are predicted simultaneously, as different clinical management would be applied according to the different mutated genes.