Construction of PDX library derived from Japanese cancer patients

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Summary in Japanese

抗がん剤開発の成功率を向上させるためには，臨床的に適切な腫瘍モデルが求められている．ヒト腫瘍を免疫不全マウスに直接移植することによって作製される患者由来の異種移植片（**PDX**）モデルは，従来のモデルよりも臨床的に適切なモデルとして広く受け入れられている．我々は，日本人の特性も加味した効率的な新薬開発を目指して，日本人がん患者由来の **PDX**（**J-PDX**）を産業活用できるよう，またさらに高度な研究・医療への応用の推進に取り組んできた．

国立がん研究センターより入手した **PDX** 腫瘍を免疫不全マウスに移植した．一定期間後に腫瘍を採取し，腫瘍片を液体窒素タンクに保存し，ライブラリーとして整備した．また，採取した腫瘍の一部は病理解析や遺伝子解析を行い，各 **PDX** の情報を収集したため，そのデータの一部を紹介する．

これらの情報を整備することは，抗がん剤の開発に使用する **PDX** の選択に非常に重要であり，新薬の開発に大いに貢献するものである．

Objective

To improve the success rate of anti-cancer drug development, clinically relevant tumor models are required. Patient-derived xenograft (PDX) tumor model, which is generated by direct implantation of human tumor into immunodeficient mice, has been widely accepted as a more clinically relevant model than conventional model. We have been promoting the application of PDX derived from Japanese cancer patients to more advanced research and medical treatment so that it can be industrially utilized with the aim of developing efficient new drugs that take into account the characteristics of Japanese people. PDX tumors obtained from the National Cancer Center (NCC) were transplanted into immunodeficient mice in the LSIM Safety Institute Corporation (LSSI). Tumors were collected and the tumor pieces were stored in liquid nitrogen tanks and maintained as libraries. In addition, some of the collected tumors were subjected to pathological analysis and gene analysis to collect information on each PDX.

Materials and Methods

Animal
Female NOG mice (NOD.Cg-*Prkdc* ^{scid}*Il2rg* ^{tm1Sug}/ShiJic) obtained from Central Institute for Experimental Animals.

PDX tumor
PDX tumors obtained from NCC and stored in a liquid nitrogen storage tanks.

Inoculation of PDX tumor
PDX tumor pieces were inoculated subcutaneously or into the mammary gland under isoflurane inhalation anesthesia. PDX tumors were inoculated to 3 animals per strain.

Measurement of tumor diameters
Tumor diameter was measured using caliper once a week. The tumor volume was calculated by the following equation.

Estimated tumor volume (mm^3) = **1/2** × **long diameter** (mm) × **short diameter** (mm) × **short diameter** (mm)

Pathological analysis
Tumor was immersed in 10% formalin neutral buffer solution, and paraffin-embedded blocks were created. Pathological analysis (histological type) was performed using HE stained tissue sections at Pathology Institute Corp.

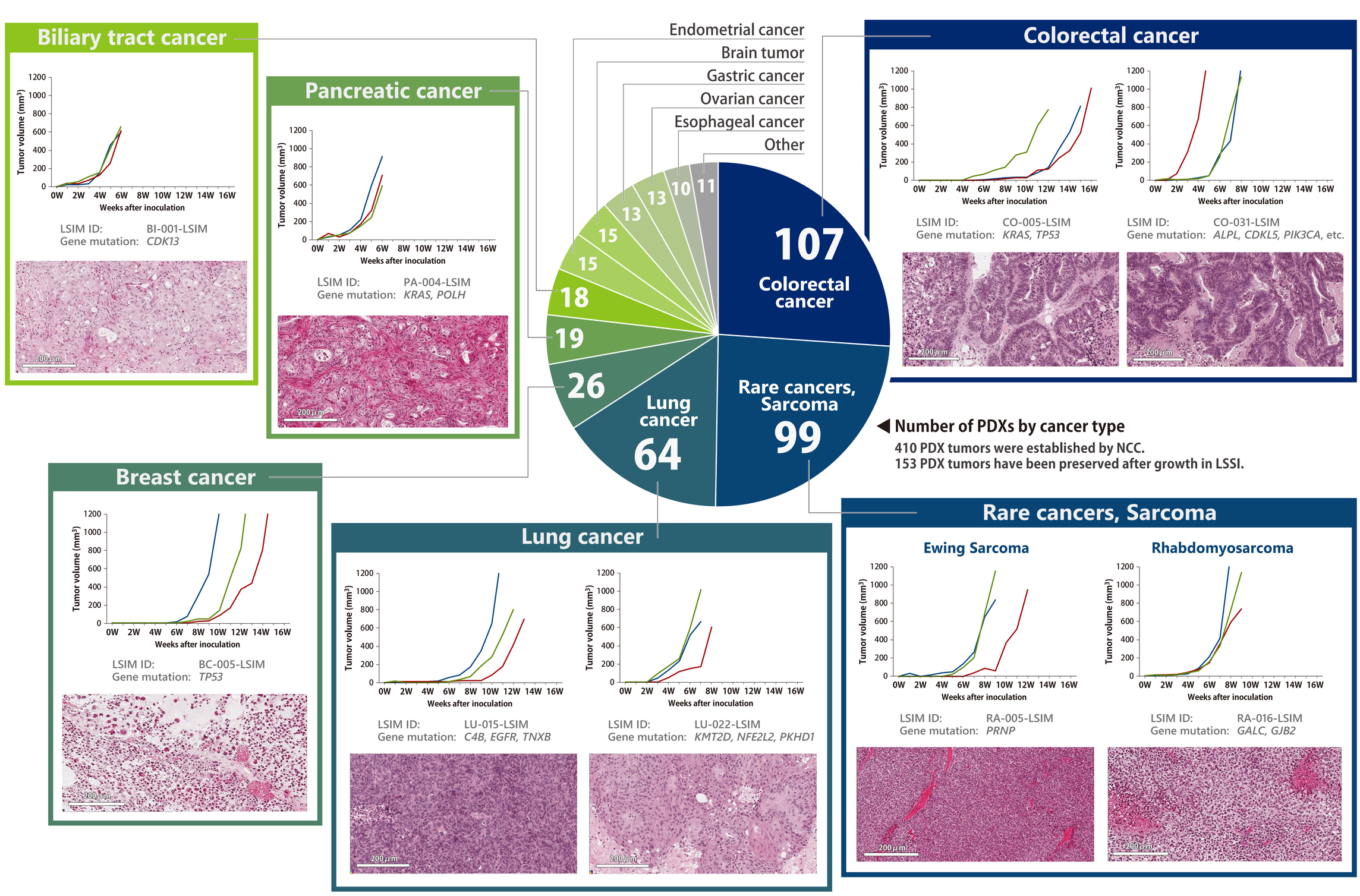
Whole exome sequencing
Tumor was snap-frozen, and RNA was extracted using AllPrep DNA/RNA 96 Kit (QIAGEN).
Whole exome sequencing was performed at Macrogen Japan Corp., and analyzed by the Genetic Analysis Research Department, LSI Medience Corp.

Conclusion

There was a large difference in the growth rate between tumors. Even in tumor pieces of the same PDX, the growth rate was different for each animal. Compared to the CDX model in which a homogeneous cell population is inoculated, the PDX model, which maintains cancer heterogeneity, tends to have greater variation in tumor growth. The present data are useful for pharmacological studies using PDXs because this variation should be taken into account when setting the number of animals in the group, and the number of inoculated animals for the required number of animals.

Results

The **red**, **blue**, and **green** lines in each graph show the growth of tumors in each animal.



Please refer to our website for PDX list, gene expression information, details of gene mutation, etc.
https://www.ankaken.co.jp/topics02.html

COI Disclosure Information

Lead Presenter: Shinichiro Tsunesumi
I have no financial relationships to disclose.