Establishment of patient derived xenograft (PDX) and PDX derived cell lines from liver-fluke associated cholangiocarcinoma tissue.

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Patient-derived xenograft (PDX) models are created by engraftment of patient's tumor tissues into immunocompetent mice. Since PDX model keep the characteristics of primary patient's tumor such as gene expression profiles and drug sensitivity, it now becomes most reliable *in vivo* human cancer model. The engraftment rate are increased with the introduction of NOD/Scid based immunocompromised mice, especially, NK cell defective NOD strains: NOD/Scid/IL2Rγ^{nu} (NOG/NSG) mice and NOD/Scid/Jak3^{null} (NOJ) mice. BALB/c Rag-2/Jak3 double deficient (BALB/c R/J) mice were also established and have been used as preferable recipient for PDX.

Liver-fluke associated cholangiocarcinoma (CCA) is a major health problem in Southeast Asia, particularly countries along the Mae Khong River. The critical obstacles of CCA diagnosis and treatment are the high heterogeneity of disease and considerable resistance to treatments. Recent multi-omics studies revealed the promising targets for CCA treatment; however, limited models for drug discovery is available. We transplanted 16 frozen CCA tissues into BALB/c R/J mice subcutaneously, and 12 CCAs (8 intrahepatic and 4 extrahepatic subtypes) were successfully grown and sub passaged in BALB/c R/J mice. Five CCA cell lines were established from 12 PDX tissues. The effects of CDK4/6 inhibitor was evaluated and confirmed in PDX model. Thus, PDX and PDX derived cell lines would be a useful platform tor precision cancer medicine.

[Awards]

1992 Japan Association for Development of Community Medicine, Research Award
1993 Japanese Society of Hematology, Young Investigator's Award
1999 Mochida Memorial Foundation for Medical and Pharmaceutical Research, Research Award
2000 Chiba University Inohana Alumni Association, Academic Award
2010 Japan Leukemia Research Fund, Research Award
2017 Kumamoto University Education Activity Award
2018 The Honorary Doctorate Degree of Medicine, Khon Kaen University, Thailand

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