Continuing the Development of Anaplastic Thyroid Cancer PDXs

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Background

Anaplastic thyroid cancer (ATC) is an extremely dangerous variation of tumors that inflicts humans with very low survival rates after a year. Although ATC makes up for a minority of thyroid cancers[3], it contributes to almost half of the annual mortality. Because ATC is usually resistant to standard chemotherapy[3], patient-derived xenograft (PDX) models are often used. With the close similarities in gene expression patterns and genetic differences. PDX models allow for a more accessible and effective assessment of drug responses.

Aim

To develop ATC PDX models in vivo to increase the number of thyroid cancer models for future use in drug and treatment.

Methodology

- Thyroid tumors from patients who were diagnosed with ATC prior to operations were collected and divided in order to develop cell lines and PDX models[1]
- In vivo mice models, the previously stated thyroid tumors were prepared into 4 x 4 x 4-mm sections and implanted into immunodeficient mice[1]
- These mice were then measured for the following weeks in order to record tumor growth volume (height x length x width)
- When tumors reached 1000 mm^3[1] volume, the mice were euthanized and the resulting tumor was divided into pieces to be used for PDX model expansion[1]
- PDX models are established when the tumors have gone through four generations (F0 to F3) [1]

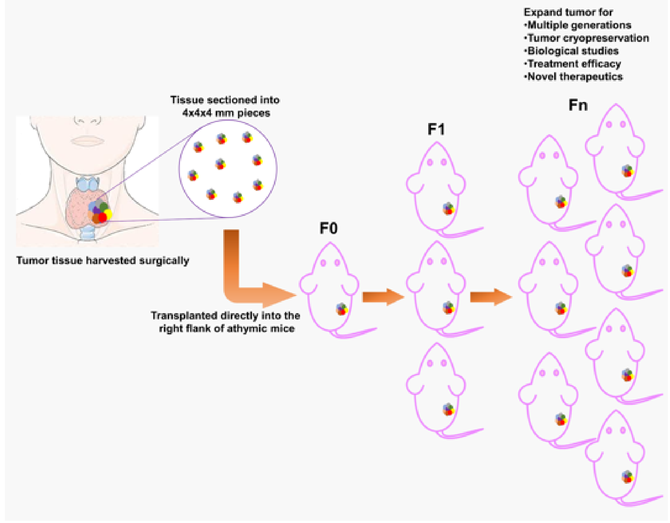

Fig. 1. Tumor from patient is prepared in 4x4x4 mm pieces to be implanted into mice

Tumor type	PDX	Tag	Date started	3/21/22	4/5/22	5/23/22	6/7/22	6/22/22	7/11/22
ATC	HOSC226F1*	367	6/21/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC226F1	200	3/29/22	n/a	n/a	23.58	80.66	79.41	58.62
ATC	HOSC227F0	128	3/7/22	n/a	81.35	70.14	59.90	No T	No T
	HOSC227F0	131	3/7/22	n/a	n/a	n/a	n/a	n/a	n/a
ATC	HOSC228F0	132	3/9/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC228F0	133	3/9/22	n/a	n/a	n/a	n/a	n/a	n/a
ATC	HOSC217F3	51	2/7/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	53	2/7/22	n/a	n/a	n/a	107.13	183.54	521.93
	HOSC217F3	55	2/7/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	326	6/14/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	333	6/14/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	334	6/14/22	n/a	n/a	n/a	n/a	n/a	87.34
	HOSC217F3	335	6/14/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	336	6/14/22	n/a	n/a	n/a	n/a	n/a	n/a
	HOSC217F3	337	6/14/22	n/a	n/a	n/a	n/a	n/a	n/a

Table 1. Recordings of various developing PDX models and tumor growth in volume (length x width x height)**.** The symbol n/a shows that no tumor was detected at the time. Figures provided by Ying Henderson

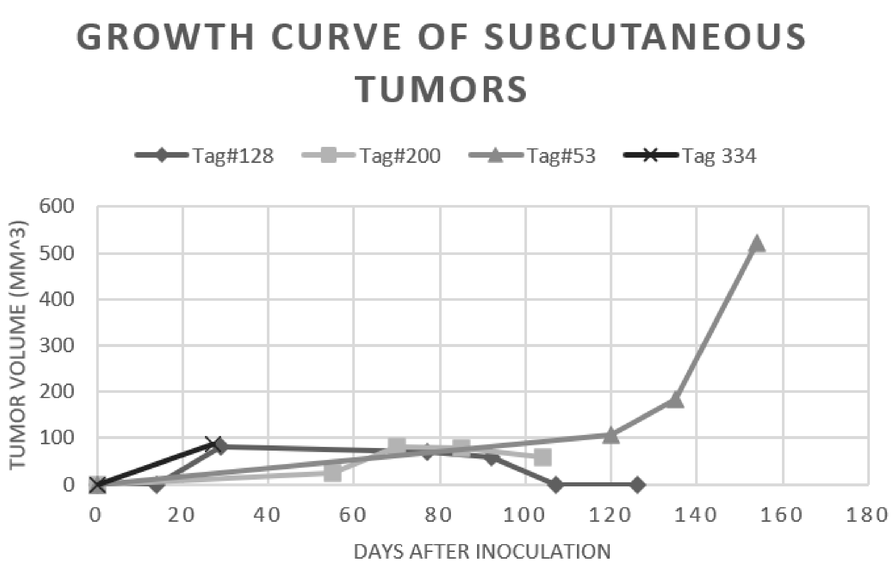

Fig. 2. Growth of tumor following initial implantation

Conclusions

Data from the experiments suggest the establishment of HOSC217 as a PDX model. While it has followed through 4 generations, from F0 to F3, and has had a presence of a tumor in one of the many mice that it was implanted in, the variable growth rate and incidence of the tumor leads to its inconclusive characterization in mice. For the one HOSC217F3 mouse that developed a large tumor of 521.93 mm^3, it faced a possibility of death because of a large decrease in its body weight and poor body shape. This led to its euthanasia and we evenly distributed its tumor to five new HOSC217F4 mice. By continuing the passage of the tumor to new generations, we hope to collect and store the HOSC217 tumor for the future. In addition, HOSC226F1 and HOSC227F0 have had some success with growing tumors, although with decreasing volumes after the initial growth. This experiment requires more time in order to further expand upon the newer PDX models, and for the tumors to grow within the mice.

Future Work

- Continue the maintenance and recording of PDX models before F3
- Continue passages of PDX models after F3 in order to store and freeze for future experiments
- Evaluate known treatments and drug combinations on the PDX model, in addition to novel ones that may be developed in the future[1]

References

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