Prize Announcement for New Fibrolamellar Carcinoma Cell Lines

Access to human fibrolamellar carcinoma (FLC) cell lines is important to accelerate research and treatment development against this lethal, rare cancer of adolescents and young adults. To address this critical need, the Fibrolamellar Cancer Foundation (FCF) seeks to create a collection of well-characterized FLC cell lines, each of which faithfully represents the biology of the tumor from which it was derived. To accelerate the accrual of a Fibrolamellar Cell Line Repository ("Collection") that will be available to the FLC research community, the FCF offers a $10,000 prize for each cell line that is approved by the FCF and deposited into the Collection as described below. This award is meant to encourage novel and creative approaches to establishing new cell lines and to enable broad access to these lines.

SUBMISSION PROCESS

Any investigator who has created a cell line derived from a human fibrolamellar carcinoma tumor is invited to submit the cell line for validation and inclusion in the Collection. Creators are encouraged to submit cell lines as soon as possible. To achieve standardization among the entire Collection, all validation experiments will be carried out in a laboratory designated by the FCF. Cell lines provided for validation will not be further distributed without the permission of the creator.

The process for submission of a cell line to the Collection is as follows:

1. Sign the accompanying Letter of Intent (Appendix A) indicating your acceptance of the terms and conditions outlined in this Prize Announcement and email it to **pcogswell@fibrofoundation.org**.
2. An FCF representative will contact you to coordinate transfer of the cell line to a designated lab for characterization and validation. If necessary, the FCF will help arrange a material transfer agreement between your institution and the designated laboratory governing the use of your cell line.
3. Cell lines must be tested for blood borne pathogens prior to receipt to establish correct Biosafety Level (BSL) handling and labeling. We recommend the Human Essential Clear Panel available from Charles River Laboratories.
4. Submit cell line(s) that have undergone at least 20 population doublings and any relevant data, tissue, or tissue derivatives to the designated repository. See Inclusion Criteria below for list of required materials and data.
5. Submit data generated on your cell line as proof of FLC characteristics.
6. Validation of the line will determine that the line is unique, human in origin, and has no mycoplasma contamination. Any data generated for the purpose of validating the cell line will be shared with you
7. If the cell line has characteristics consistent with FLC and viability for research purposes, then it will be considered for inclusion in the Collection. You will be notified in writing by the FCF whether or not your cell line(s) were selected for inclusion in the Collection.
8. Once your cell line is selected for inclusion in the Collection, the next step will be for you or your institution to execute the FCF Fibrolamellar Cancer Cell Line Collection Material Deposit Agreement or another agreement approved in writing by the FCF to deposit your cell line our designated lab or central repository.
9. Upon finalizing the Deposit Agreement and depositing the cell line into the Collection, the FCF will issue an award letter and payment form offering you an unrestricted prize for scientific and educational purposes in the amount of $10,000 for the cell line deposited into the Collection.

10. Once you complete and return the payment form, the FCF will mail a check to the "Fiscal Officer" address indicated on the payment form.

    If you have questions about any aspect of this prize, please email **pcogswell@fibrofoundation.org**.

SUBMISSION REQUIREMENTS

For a cell line to be considered for inclusion in the Collection, the following must be submitted:

1. At least two frozen vials containing the cryopreserved cell line
2. A completely de-identified pathology report from the tumor of origin
3. A copy of the signed informed consent form authorizing collection of the tumor specimen from which the cell line was derived. The informed consent must allow for the use, storage, and distribution of the cell line for all research and development purposes and be clear that no profit from any commercial products derived from the cell line will be returned to the patient.
4. A description of cell line including
    a. initial tumor dissociation and culture method
    b. approximate number of passages
    c. time period over which cells were passaged
    d. any significant changes in phenotype or emergence of subpopulations during passage
    e. history of microbial contamination
5. Instructions for culturing the cell line including product information for media and any other reagents.
6. Information about the tumor from which the cell line was derived
    a. Anatomic location of the FLC
    b. Whether the tumor was primary, or recurrent
    c. Date tumor was resected or ascites fluid containing cancer cells was collected
    d. Indicate if a portion of the tumor or ascites fluid sample was also preserved
7. Information about the patient from which the cell line was derived
    a. Demographics: gender, age at diagnosis, ethnicity
    b. Treatment history, including prior surgery, chemotherapy, immunotherapy, or radiation (if available)
    c. Patient outcome if known
    d. Is the patient alive or deceased?

<u>The following items are requested but not required</u>

1. Several unstained slides from the tumor or cell sample from which the cell line was derived
2. A frozen and/or paraffin embedded tissue sample from the tumor of origin and/or nucleic acids derived from the tumor of origin
3. Normal tissue, peripheral blood mononuclear cells and/or non-tumor DNA from the patient from which the tumor was derived is strongly encouraged to discern somatic from inherited mutations
4. Any available data regarding phenotype (e.g., growth in soft agar or xenografts), genotype, copy number changes, gene expression, protein expression, or other validation experiments conducted on the purported FLC cell line.

INCLUSION CRITERIA

Cell lines can be propagated as cells attached to culture vessels or in three-dimensional culture. Stable "tumor organoids," potentially including a minority population of mesenchymal/tumor stromal cells in addition to cancer cells, will be accepted if they meet the inclusion criteria. Lines must retain characteristic features of FLC, including the *DNAJB1-PRKACA* fusion gene (for classic FLC), or other relevant markers such as loss of *PRKAR1A*, or genomic abnormalities consistent with "hepatocellular carcinoma with fibrolamellar-like features." A cell line may be initiated from a specimen taken directly from a patient or after propagation of tumor cells in a PDX model. Cell lines should be developed from independent specimens, usually from different patients. However, multiple cell lines derived from the same patient but grown from specimens obtained at different times (e.g., from a primary tumor and after a recurrence) or from different metastatic deposits will be considered. Each cell line will be evaluated for inclusion in the Collection based on the following criteria:

Criterion	Assay
All Required	

Confirmed FLC diagnosis of source tumor	• Histology
	  ○ Morphology
	  ○ Ideally, dually positive for cytokeratin 7 and CD68 by immunohistochemistry
	• Ideally, molecular and/or cytogenetic (e.g., break-apart FISH assay) analysis

Human species	Karyotype, human-specific PCR product, or hybridization to human oligonucleotide array
Rearranged genome	Karyotype, CGH, aCGH, or SNP array
Cell line retains *DNAJB1-PRKACA* gene fusion (typical FLC); or other molecular abnormalities consistent with FLC or HCC with FLC-like features	RNA sequencing, cytogenetic analysis, or DNA sequencing Confirmation of identity with molecular driver(s) of initial tumor, when available
Exhibits acceptable doubling rate	Doubling rate of 12 days or less
Cell line growth	At least 20 population doublings in culture [e.g., ca. 9 passages at 1:5 dilution]

PRIZE GUIDELINES AND EXPECTATIONS

In addition to satisfaction of the above scientific criteria, the FCF has the following guidelines and expectations for cell lines to be included in the Collection.

- Proper consent from the patient must have been obtained to allow for the use, storage, and distribution of the cell line for all research and development purposes. No profit from any commercial products derived from the cell line(s) shall be returned to the patient.
- Data generated in characterizing the cell line will be shared only with the creator and the FCF. This data will be kept confidential unless the creator waives this confidentiality. Upon inclusion in the Collection and acceptance of the prize, all properly deidentified data associated with the cell line provided to the FCF will be made public and distributed with the cell line.
- The FCF encourages creators to publish results of the research leading to the development and characterization of the new cell line(s), preferably in a peer-reviewed open access journal. Therefore, at the request of the creator, the FCF will embargo specific data generated in characterizing the cell line for up to six months to give the creator an opportunity to publish on the creation and characterization of the cell line.
- You or your institution must have entered into a Deposit Agreement with the FCF for purposes of depositing your cell line into the Collection.
- Upon acceptance of the prize, the FCF will be permitted to publicize the name of the institution and/or creator, and the amount of the prize.

TERMS AND CONDITIONS OF PRIZE

1. AWARDS PROCESS

   The decision to include a cell line in the Collection and to award a $10,000 prize to the cell line's creator will be made by the FCF Board of Directors based on the recommendation of expert advisors, the availability of funding, and other pertinent factors. The FCF will consider the genetic and biological characteristics of the cell line, as well as accompanying data regarding the tumor from which the cell line was derived. Investigators will be notified in writing by the FCF whether cell line(s) are selected or not for inclusion in the Collection. Upon validation, selection for inclusion in the Collection, execution of the Deposit Agreement and deposit of the cell line with the FCF designated repository, the FCF will issue an award letter and payment form offering an unrestricted prize for scientific and educational application in the amount of $10,000 for the cell line deposited into the Collection.

2. ACCEPTANCE OF AWARD

   A grantee indicates acceptance of an award and will become bound by the terms and conditions attached to the award notification letter by signing the award notification letter and depositing funds disbursed by the FCF. Each prize will be awarded on the terms and conditions outlined herein.

3. DISBURSEMENT POLICY

   This prize is made to reward the creator of an FLC cell line for contributing that cell line to the FCF Cell Line Collection. The prize is made as an unrestricted award to the creator's institution to be used at the sole discretion of the creator for scientific and educational application. Payment to the creator's institution will be made by check unless otherwise requested by an authorized institutional official. Checks will be mailed to the "Fiscal Officer" address indicated on the payment form.

4. LIABILITY

   Upon acceptance of this award, the creator and the creator's institution will indemnify and hold harmless the FCF, its Board, officers, agents, advisors and constituents from any claim, judgment, award, damage, settlement, liability, negligence, or malpractice arising from research or investigation activities related to this award.

Appendix A

Intent to Submit Cell Lines for Inclusion in Fibrolamellar Cancer Foundation Cell Line Collection

I have read and agree to the terms and conditions of the Fibrolamellar Cancer Foundation Repository ("Collection") set forth in the Prize Announcement and intend to submit the cell line(s) named as follows to be considered for inclusion in this Collection:

[insert names of cell line(s)]_____

I will make these cell line(s) available to the FCF for the purposes of characterization and validation. I understand that data generated on my cell line(s) will be shared with me and with the FCF to serve as a basis for the decision whether to accept my cell line(s) for inclusion in the Collection. I understand that inclusion in the Collection is not guaranteed and is determined by the FCF Board of Directors based on the characterization of the cell line, the availability of funding, and other pertinent factors.

If my cell line(s) are selected for inclusion in the Collection, then, as a condition to my receipt of any corresponding award from the FCF, I will deposit my cell line(s) with the designated repository under Deposit Agreement approved by the FCF to use, store and distribute this cell line(s) for all research and development purposes.

Name _____

Job Title _____

Organization _____

Address _____

Telephone # _____

Email Address _____

_____

Investigator's Full Name (typed)

_____ _____

Signature **Date**