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GP-*write*

Pilot Project Proposal
(Not to exceed two pages)

Name of Project: UltraSafe Cell Line

Proposer and Contact Information:
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Background:
There is an unmet need for an "Ultrasafe human cell line" designed to serve as a platform for many biomedical applications, from production of biologics, to modeling cell and tissue behaviors, to actual ex vivo and ultimately in vivo therapeutic applications.

Technical Idea:
We propose to engineer a human cell line for use as a basic and potentially universal platform for human biotechnology. This can be done by altering roughly 1% of the genome, including the exons of all of the genes, and nearby sequences, leaving the vast majority of the noncoding regions, which are at this point far less well understood, untouched.

It is anticipated that many of the details of this cell line remain to be extensively discussed and the plans for exactly how to construct it will be jointly worked out by a group of experts in human genetics and genomics as well as synthetic genomicists.

Utility and "Fit" For GP-write:
This cell line will be engineered to be ultrasafe from many distinct perspectives. Because this cell line would potentially be of great value to the pharmaceutical, vaccine, and biotechnology industries, this theme as a pilot project should be very attractive to philanthropic and industry, potentially as a public/private partnership designed to benefit the entire biomedical community. This approach would in theory allow a launch of the project without NIH support, which might be desirable in a time of unprecedented NIH budget cuts.

Safety and other properties of an “Ultrasafe” cell line

Property	Explanation
Virus resistant	Cell line resists viruses through sense codon/tRNA recoding
Prion resistant	Endogenous prion gene deleted or recoded
Retroelement/transposon free	All mobile DNAs inactivated
Triplet repeat resistant	Triplet repeat regions made safe by recoding
Germ line negative	Engineered to prevent germ line transmission
Radiation resistant	Very active DNA Repair systems
Multiple self destruct circuits	Orthogonal mechanisms to control cell growth
Cancer resistant	P53 and other tumor suppressors re-engineered to minimize chance of deleterious mutations
Immuno-negative	Engineered to minimize immune rejection
Multiple safely targetable sites	Safe insertion of future engineered circuits and pathways
Major allele for every SNP and indel	“Universal” human cell maximizes compatibility with diverse humans
Scramble-able	Allows rapid evolutionary optimization for desirable traits