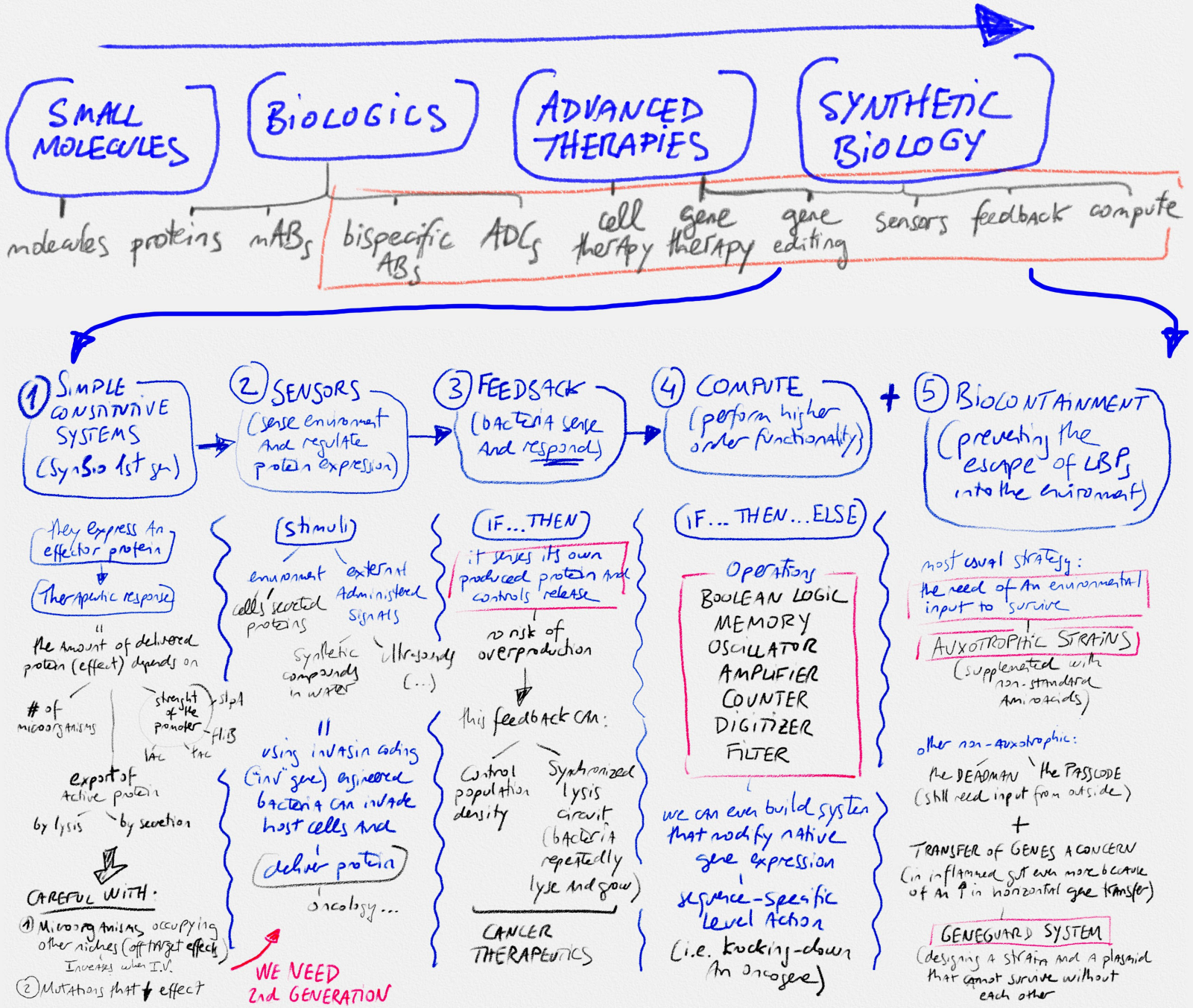
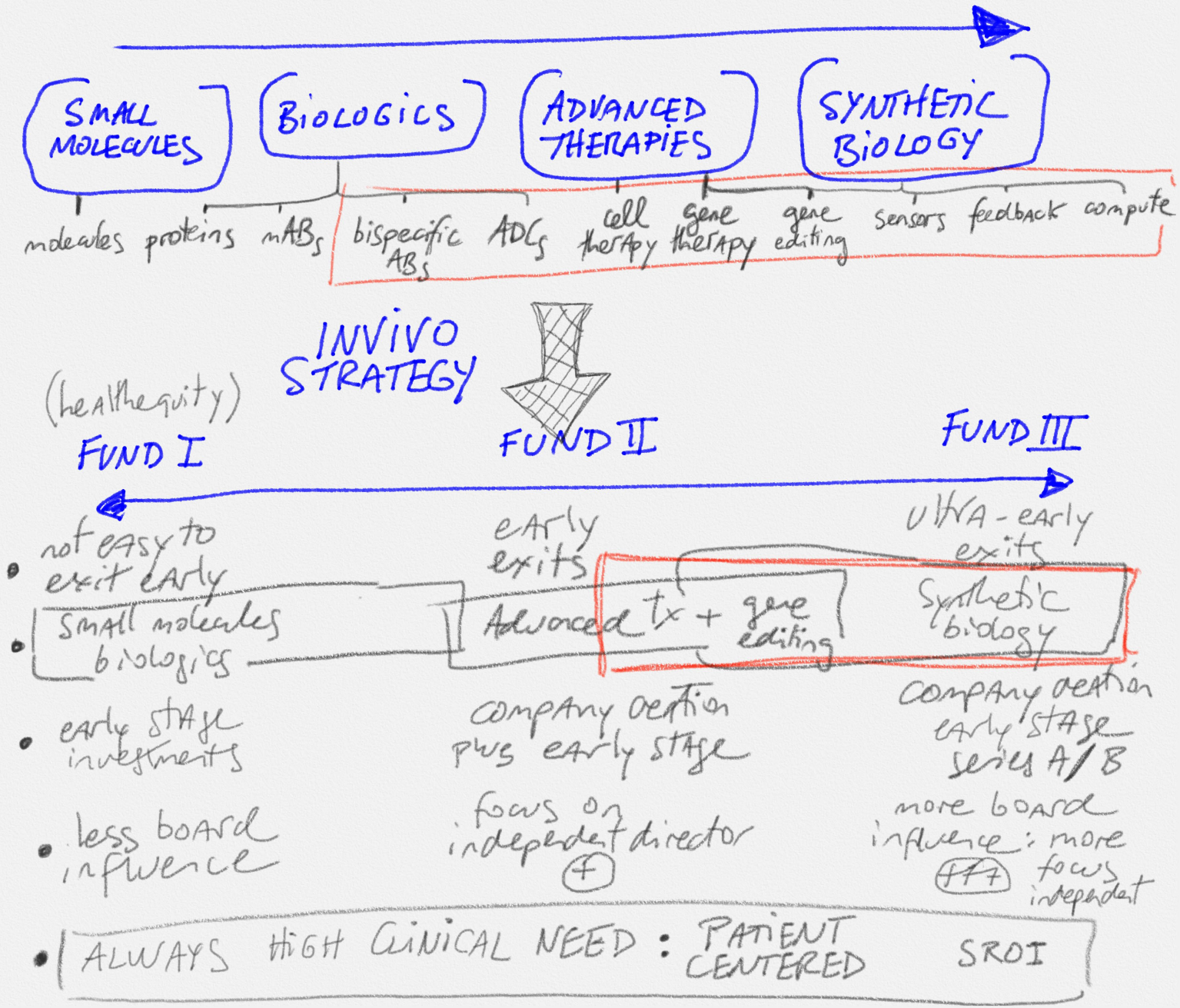

SMALL MOLECULES
BIOLOGICS
ADVANCED THERAPIES
SYNTHETIC BIOLOGY
molecules
proteins
mABs
bispecific ABs
ADCs
cell therapy
gene therapy
gene editing
sensors
feedback
compute
1 SIMPLE CONSTITUTIVE SYSTEMS (Syn3.0 1st gen)
2 SENSORS (sense environment and regulate protein expression)
3 FEEDBACK (bacteria sense and respond)
4 COMPUTE (perform higher order functionality)
+
5 BIOCONTAINMENT (preventing the escape of LBPs into the environment)
they express an effector protein
therapeutic response
"
the amount of delivered protein (effect) depends on
of microorganisms
strength of the promoter
slpA
flhD
lac
tac
export of active protein
by lysis
by secretion
CAREFUL WITH:
1) Microorganisms occupying other niches (off target effects)
Increases when I.V.
2) Mutations that ↓ effect
stimuli
environment
cells' secreted proteins
external
Administered signals
Synthetic compounds in water
Ultrasound
(...)
"
using invasin coding (inv gene) engineered bacteria can invade host cells and
deliver protein
oncology...
WE NEED 2nd GENERATION
IF...THEN
it senses its own produced protein and controls release
↓ risk of overproduction
this feedback can:
Control population density
Synchronized lysis circuit (bacteria repeatedly lyse and grow)
CANCER THERAPEUTICS
IF...THEN...ELSE
Operations
BOOLEAN LOGIC
MEMORY
OSCILLATOR
AMPLIFIER
COUNTER
DIGITIZER
FILTER
we can even build system that modify native gene expression
sequence-specific level action
i.e. knocking-down an oncogene
most usual strategy:
the need of an environmental input to survive
AUXOTROPHIC STRAINS
(supplemented with non-standard Aminoacids)
other non-auxotrophic:
the DEADMAN
the PASSCODE
(still need input from outside)
+
TRANSFER of GENES A CONCERN
(in inflamed gut even more because of an ↑ in horizontal gene transfer)
GENEGUARD SYSTEM
(designing a strain and a plasmid that cannot survive without each other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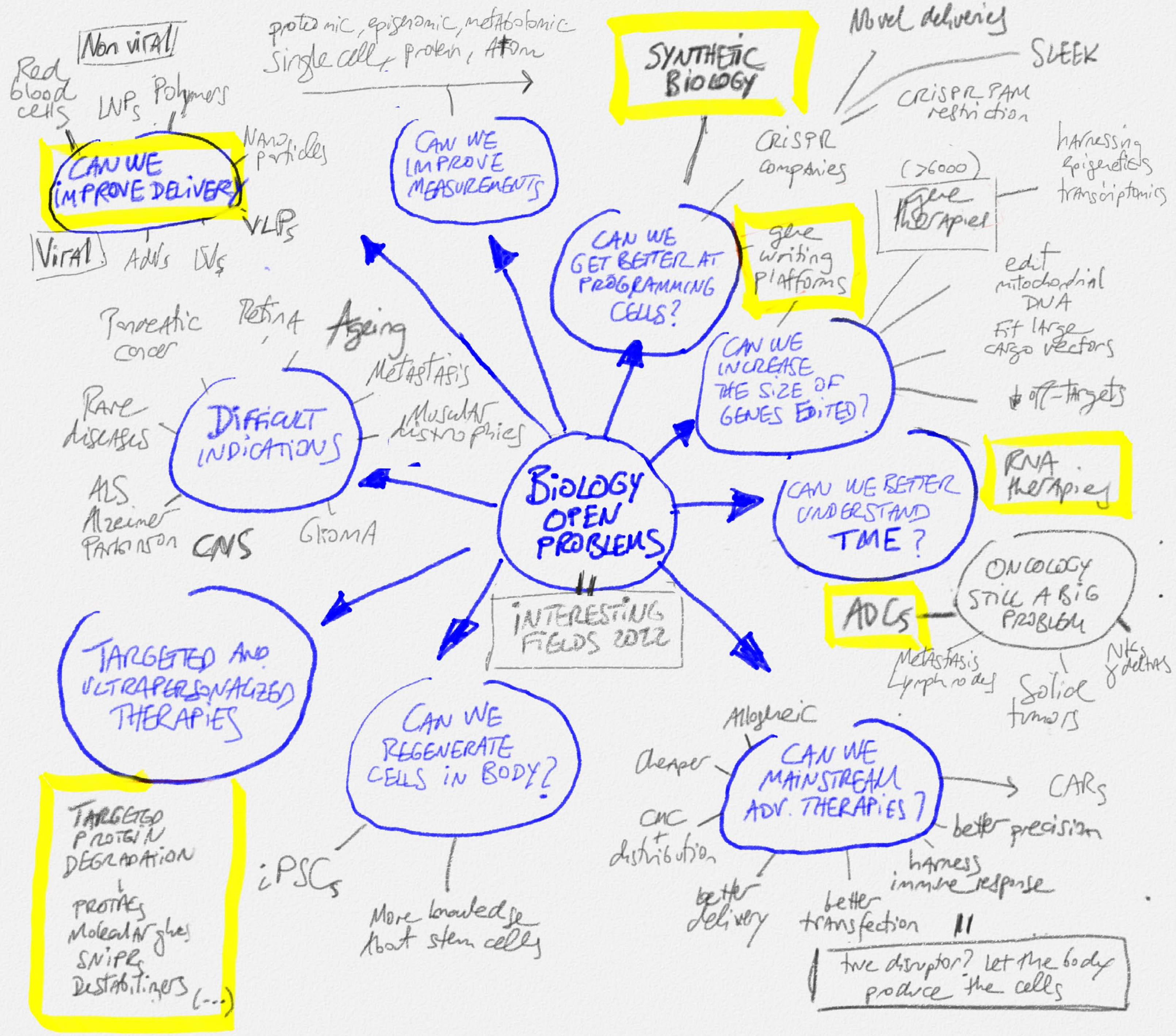
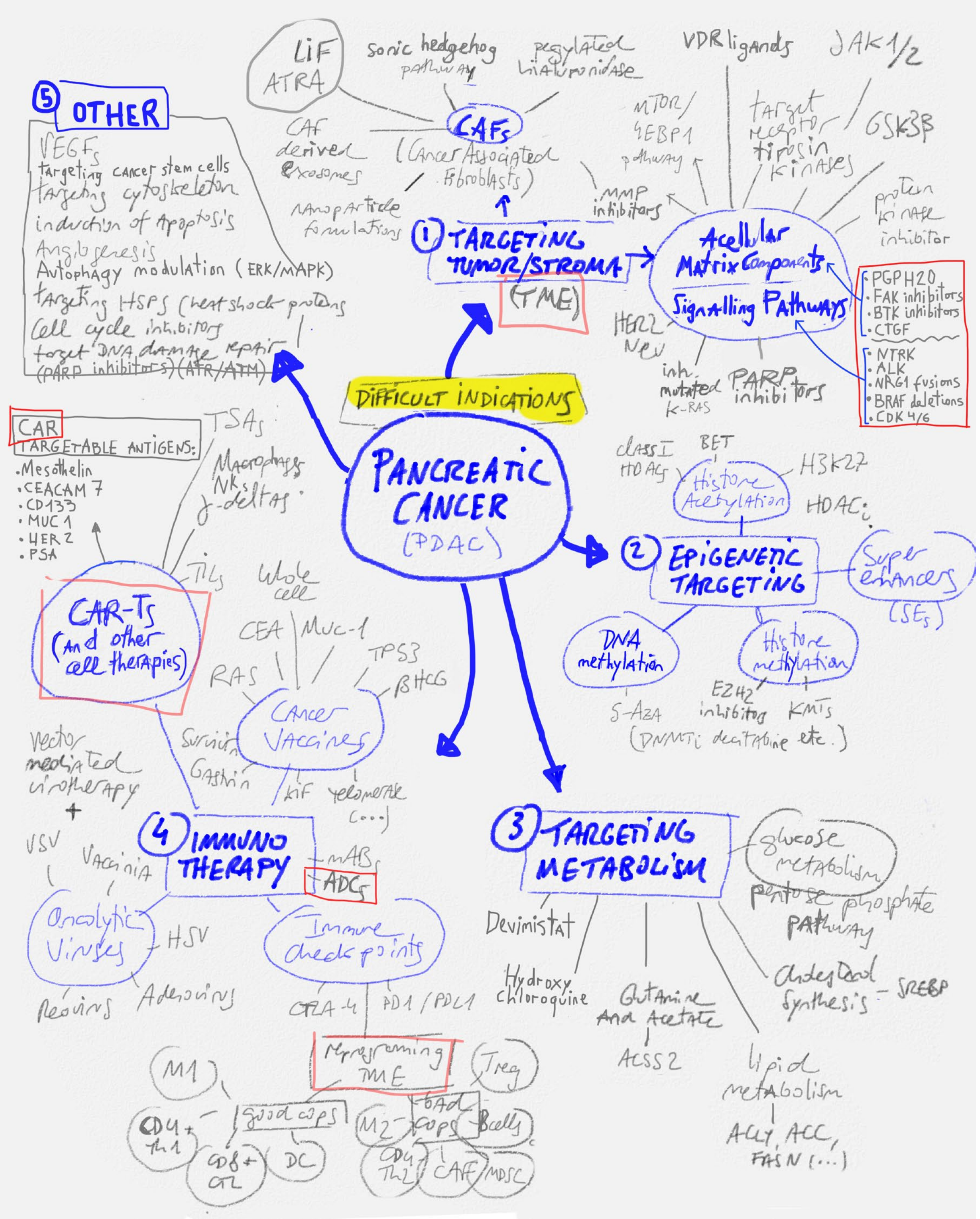
INVIVO STRATEGY
(healthequity)
FUND I
FUND II
FUND III
not easy to exit early
small molecules biologics
early stage investments
less board influence
early exits
Advanced tx + gene editing
company creation plus early stage
focus on independent director
+
ultra-early exits
Synthetic biology
company creation early stage series A/B
more board influence: more focus independent
ALWAYS HIGH CLINICAL NEED: PATIENT CENTERED
SROI



BIOLOGY OPEN PROBLEMS
=
INTERESTING FIELDS 2022
CAN WE IMPROVE DELIVERY
Non viral
Red blood cells
LNPs
Polymers
Nano particles
Viral
AAVs
LVs
VLPs
CAN WE IMPROVE MEASUREMENTS
proteomic, epigenomic, metabolomic
Single cell, protein, Atom
SYNTHETIC BIOLOGY
CAN WE GET BETTER AT PROGRAMMING CELLS?
CRISPR companies
Novel delivery
SLEEK
CRISPR PAM restriction
gene writing platforms
(>6000)
gene therapies
harnessing epigenetics transcriptomics
CAN WE INCREASE THE SIZE OF GENES EDITED?
edit mitochondrial DNA
fit large cargo vectors
↓ off-targets
CAN WE BETTER UNDERSTAND TME?
RNA therapies
ONCOLOGY STILL A BIG PROBLEM
ADCs
Metastasis Lymph nodes
Solid tumors
NKs γ deltas
DIFFICULT INDICATIONS
Pancreatic cancer
Retina
Ageing
Metastasis
Muscular distrophies
Rare diseases
ALS
Alzeimer
Parkinson
CNS
GLIOMA
TARGETED AND ULTRAPERSONALIZED THERAPIES
TARGETED PROTEIN DEGRADATION
PROTACs
Molecular glues
SNIPRs
Destabilizers (...)
CAN WE REGENERATE CELLS IN BODY?
iPSCs
More knowledge about stem cells
CAN WE MAINSTREAM ADV. THERAPIES?
Allogeneic
Cheaper
CMC + distribution
better delivery
better transfection
harness immune response
better precision
CARs
=
true disruptor? let the body produce the cells

Example:



PANCREATIC CANCER (PDAC)
DIFFICULT INDICATIONS
1 TARGETING TUMOR/STROMA (TME)
CAFs (Cancer Associated Fibroblasts)
LIF
ATRA
sonic hedgehog pathway
pegylated hyaluronidase
VDR ligands
JAK 1/2
GSK3β
CAF derived exosomes
nanoparticle formulations
MMP inhibitors
mTOR/4EBP1 pathway
target receptor tyrosin kinases
protein kinase inhibitor
Acellular Matrix Components
Signalling Pathways
PGPH20
FAK inhibitors
BTK inhibitors
CTGF
NTRK
ALK
NRG1 fusions
BRAF deletions
CDK 4/6
HER2 Neu
inh. mutated K-RAS
PARP inhibitors
2 EPIGENETIC TARGETING
Histone Acetylation
class I HDACs
BET
H3K27
HDACi
Super enhancers (SEs)
DNA methylation
5-AZA (DNMTi decitabine etc.)
Histone methylation
EZH2 inhibitors
KMTs
3 TARGETING METABOLISM
glucose metabolism
pentose phosphate pathway
cholesterol synthesis
SREBP
lipid metabolism
ACLY, ACC, FASN (...)
Devimistat
Hydroxy Chloroquine
Glutamine and Acetate
ACSS2
4 IMMUNO THERAPY
mABs
ADCs
Immune checkpoints
CTLA-4
PD1/PDL1
Reprogramming TME
M1
Treg
CD4+ Th1
CD8+ CTL
DC
good cops
bad cops
M2
B cells
CD4 Th2
CAF
MDSC
Oncolytic Viruses
VSV
Vaccinia
HSV
Adenovirus
Reovirus
vector mediated virotherapy
+
Cancer Vaccines
RAS
CEA
Muc-1
TP53
βHCG
Survivin
Gastrin
KIF
telomerase (...)
Whole cell
CAR-Ts (And other cell therapies)
TILs
TSAs
Macrophages
NKs
γδ-T cells
CAR TARGETABLE ANTIGENS:
Mesothelin
CEACAM 7
CD133
MUC 1
HER 2
PSA
5 OTHER
VEGFs
targeting cancer stem cells
targeting cytoskeleton
induction of Apoptosis
Angiogenesis
Autophagy modulation (ERK/MAPK)
targeting HSPs (heat shock proteins)
Cell cycle inhibitors
target DNA damage repair (PARP inhibitors) (ATR/ATM)