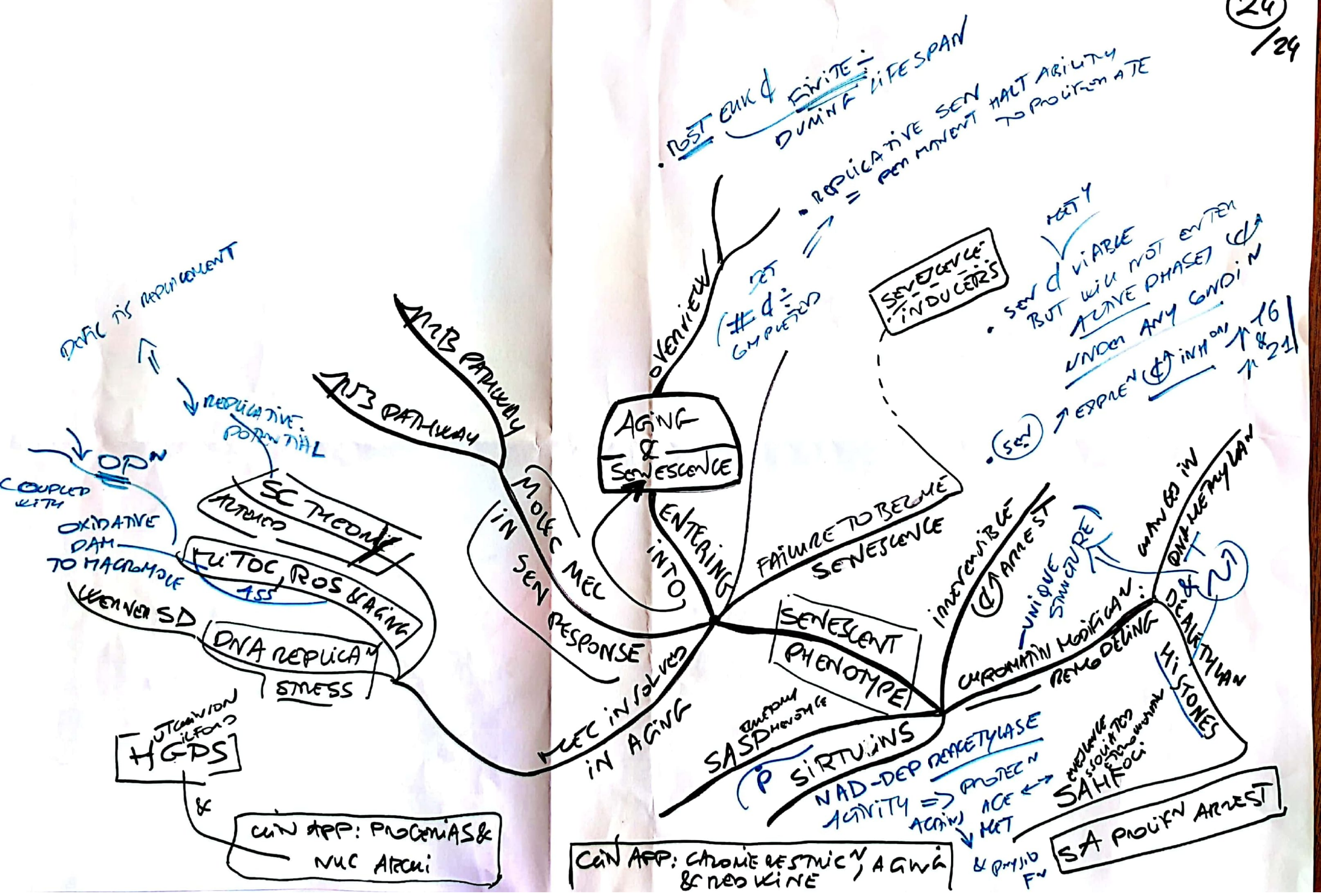
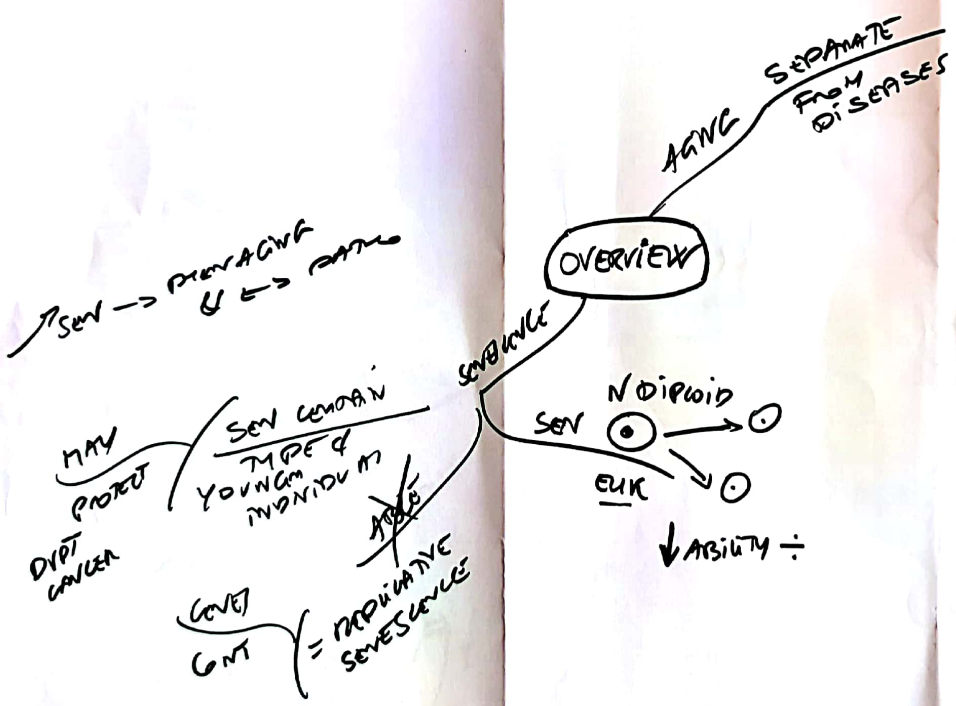
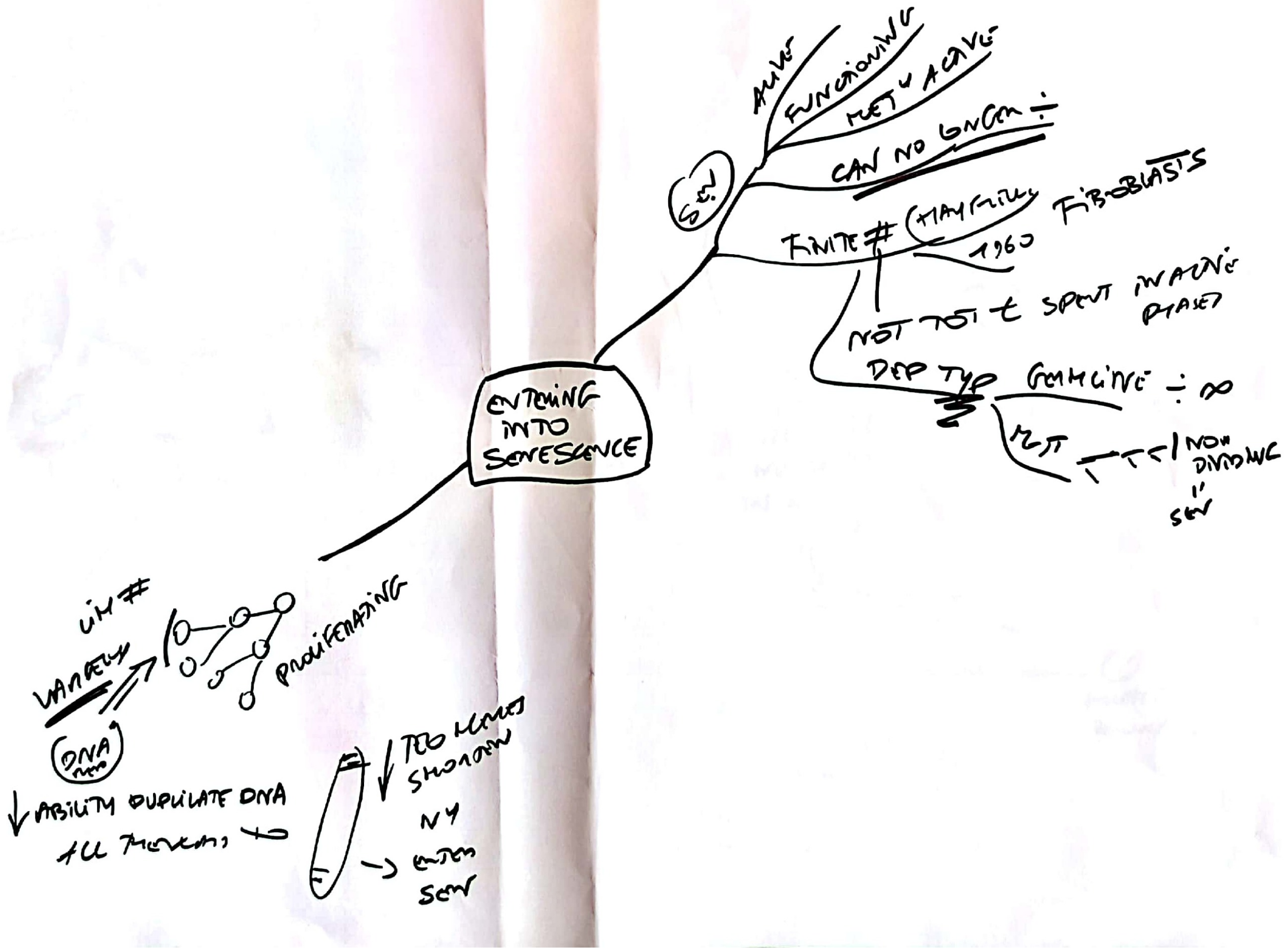
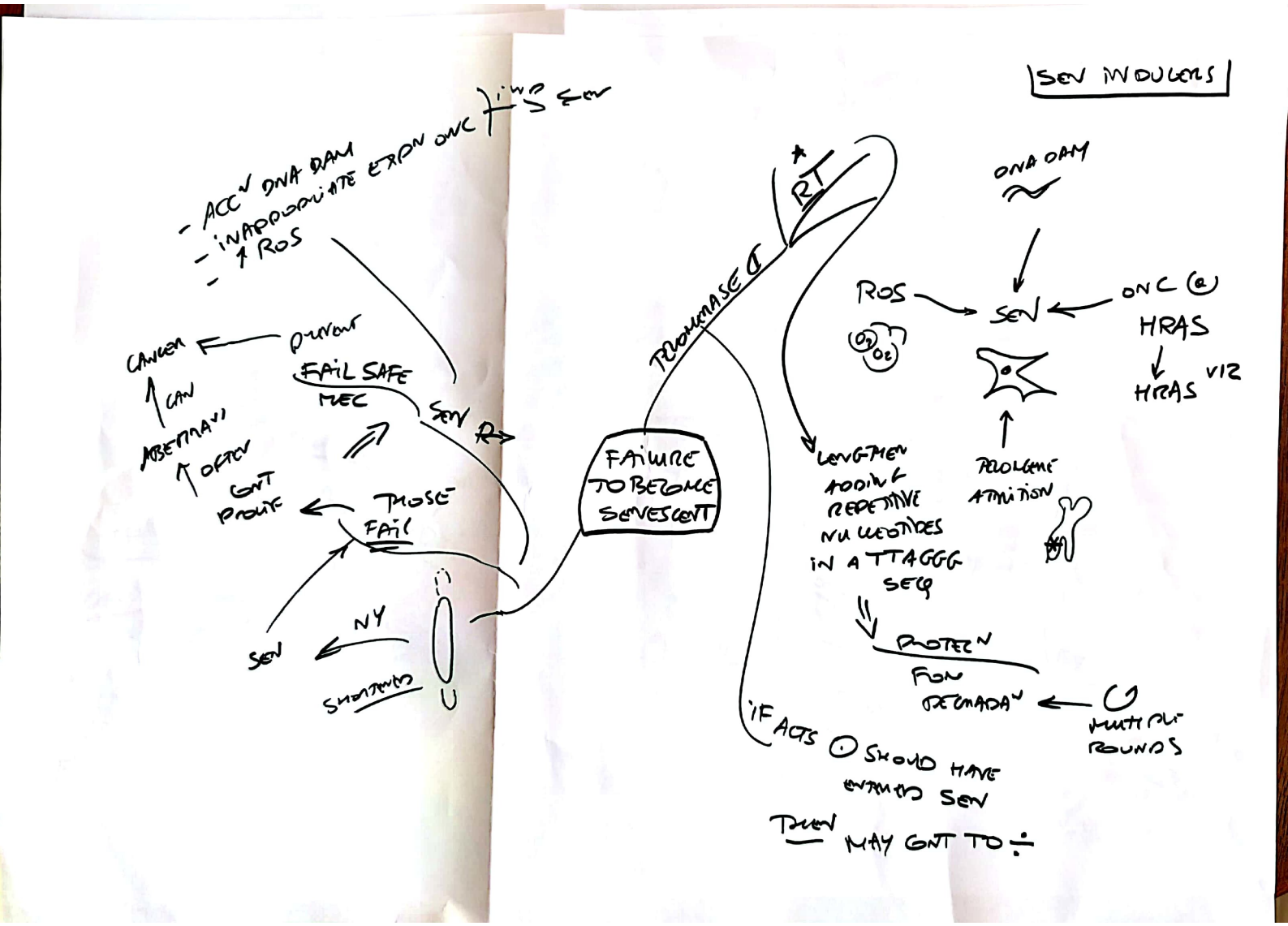
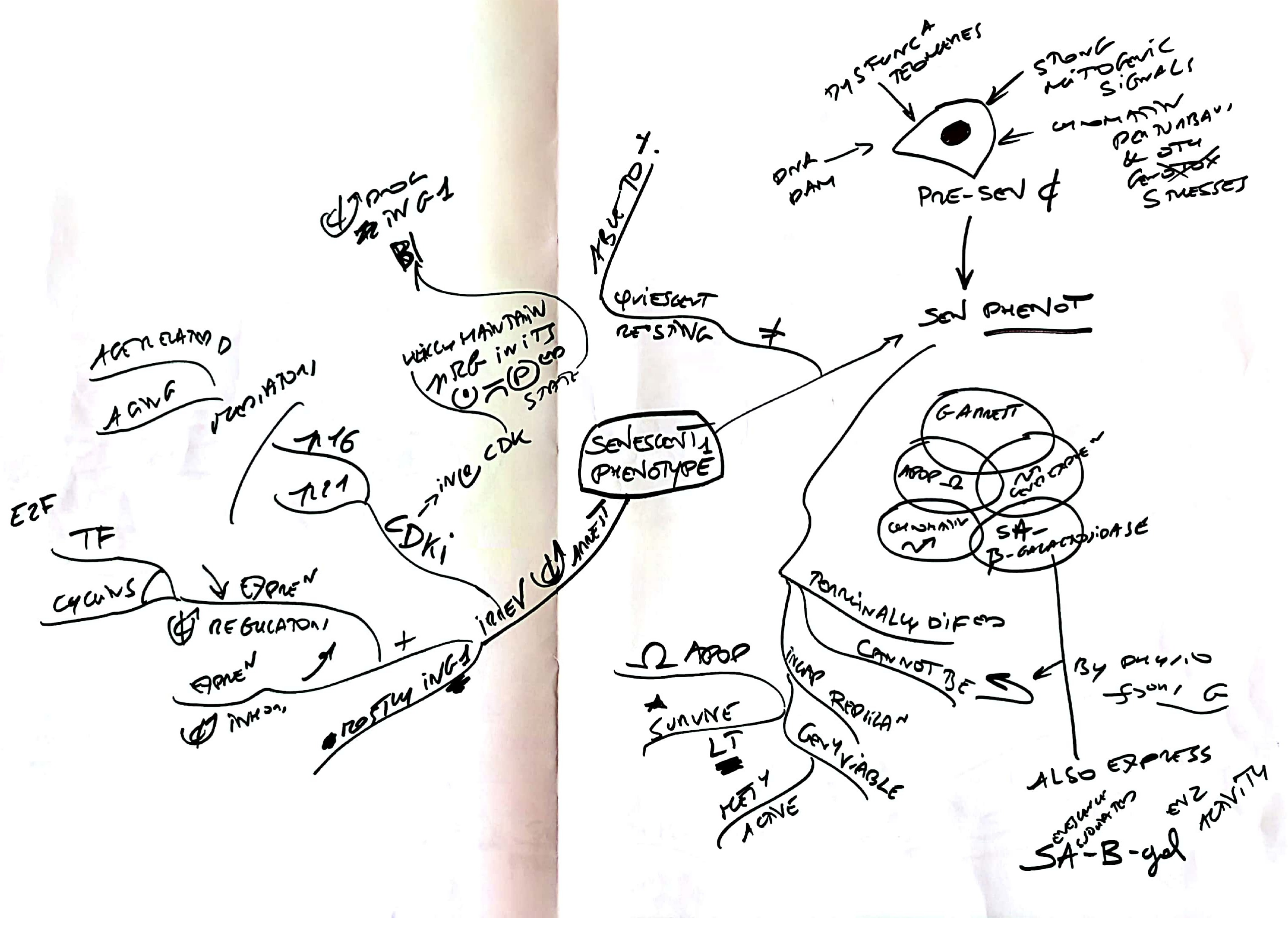

AGING & SENESCENCE
OVERVIEW
POST MIT ¢ FINITE DURING LIFESPAN
REPLICATIVE SEN = PERMANENT HALT ABILITY TO PROLIFERATE
DET # ¢ ÷ COMPLETED
SENESCENCE INDUCERS
SEN ¢ VIABLE BUT WILL NOT ENTER ACTIVE PHASES ¢¢ UNDER ANY CONDI N
SEN ↑ EXPRE N ¢ INH ORS ↑16 & ↑21
ENTERING INTO
FAILURE TO BECOME SENESCENCE
SENESCENT PHENOTYPE
IRREVERSIBLE ¢ ARREST
UNIQUE STRUCTURE
CHROMATIN MODIFICAN: REMODELING
CHANGES IN DNA METHYLAN & DEACETYLAN HISTONES
SAHF
SA PROLIF N ARREST
SASP
SIRTUINS
NAD-DEP DEACETYLASE ACTIVITY => PROTEC N
MOLEC MEC IN SEN RESPONSE
MEC INVOLVED IN AGING
SC THEORY
DNA REPLICA N STRESS
WERNER SD
HGPS
CLIN APP: PROGERIAS & NUC ARCHI
CLIN APP: CALORIE RESTRIC N, AGING & MEDICINE
REPLICATIVE POTENTIAL
OXIDATIVE DAM. TO MACROMOLE

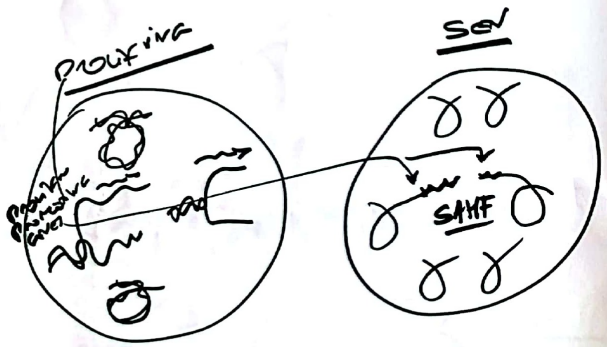

OVERVIEW
AGING
SEPARATE FROM DISEASES
SENESCENCE
SEN
N DIPLOID
EUK
↓ ABILITY ÷
SEN REMAIN
TYPE &
YOUNGER INDIVIDUALS
MAY
PROTECT
DVPT
CANCER
CONT
= REPLICATIVE SENESCENCE
SEN → PRO-AGING


ENTERING INTO SENESCENCE
SEN
ALIVE
FUNCTIONING
CAN NO LONGER ÷
FINITE #
1960
FIBROBLASTS
PHASE
GERMLINE ÷ ∞
NON DIVIDING
SEN
LIM #
VARIETY
PROLIFERATING
DNA
↓ ABILITY DUPLICATE DNA
SHORTEN
ENTER
SEN

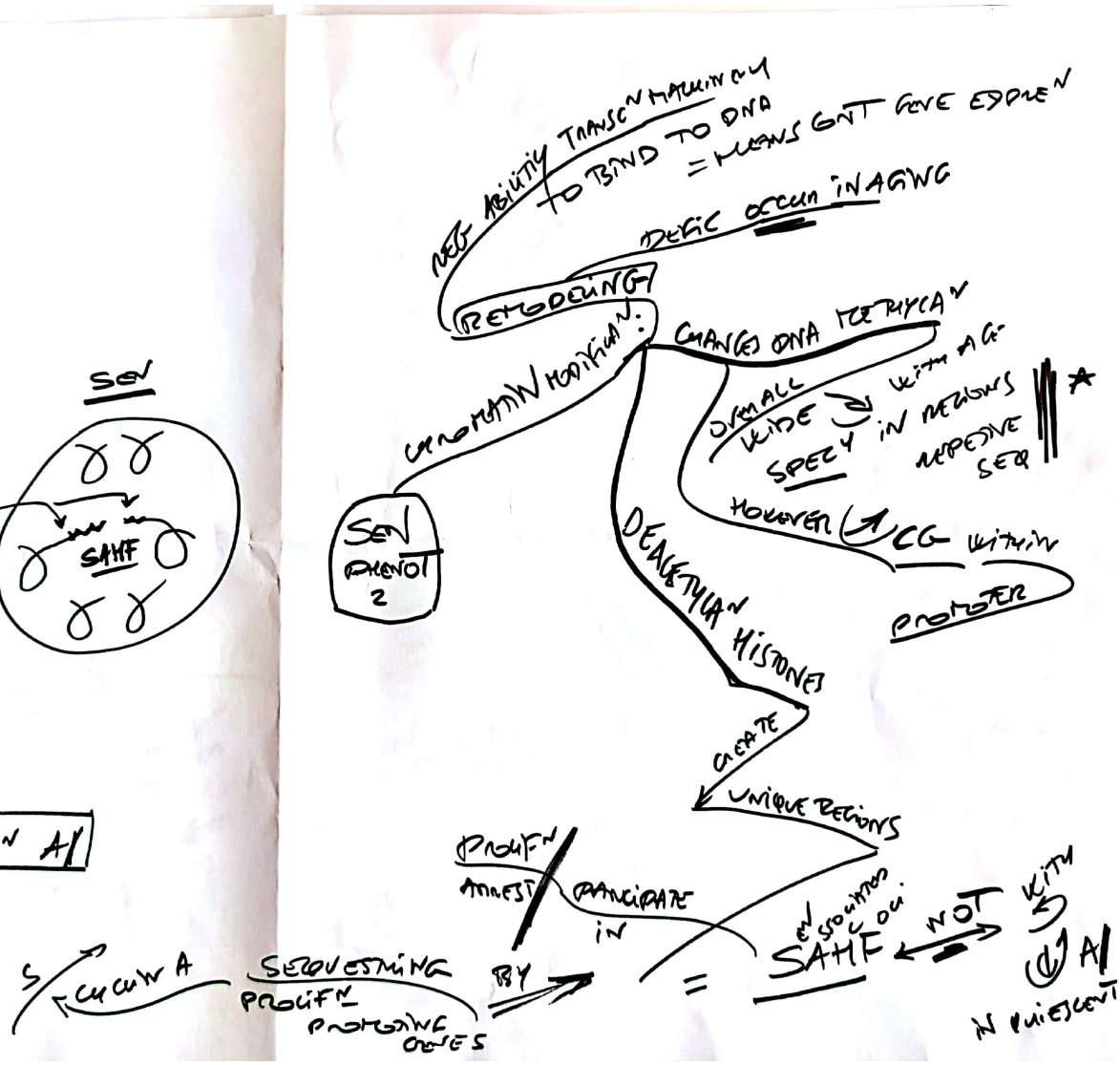

SEN INDUCERS
- ACC'N DNA DAM
- INAPPROPRIATE EXPN ONC
- ↑ ROS
CANCER
DRIVER
FAIL SAFE
MEC
SEN
CAN
ABERRANT
OFTEN
GNT
PROLIF
THOSE
FAIL
SEN
NY
SHORTENED
FAILURE TO BECOME SENESCENT
TELOMERASE
RT
ROS
SEN
ONC (a)
HRAS
HRAS V12
DNA DAM
LENGTHEN
ADDING
REPETITIVE
NUCLEOTIDES
IN A TTAGGG
SEQ
TELOMERE ATTRITION
PROTEIN
FOR
REMADAY
MULTIPLE
ROUNDS
IF ACTS ⊙ SHOULD HAVE
ENTERED SEN
THEN
MAY GNT TO ÷

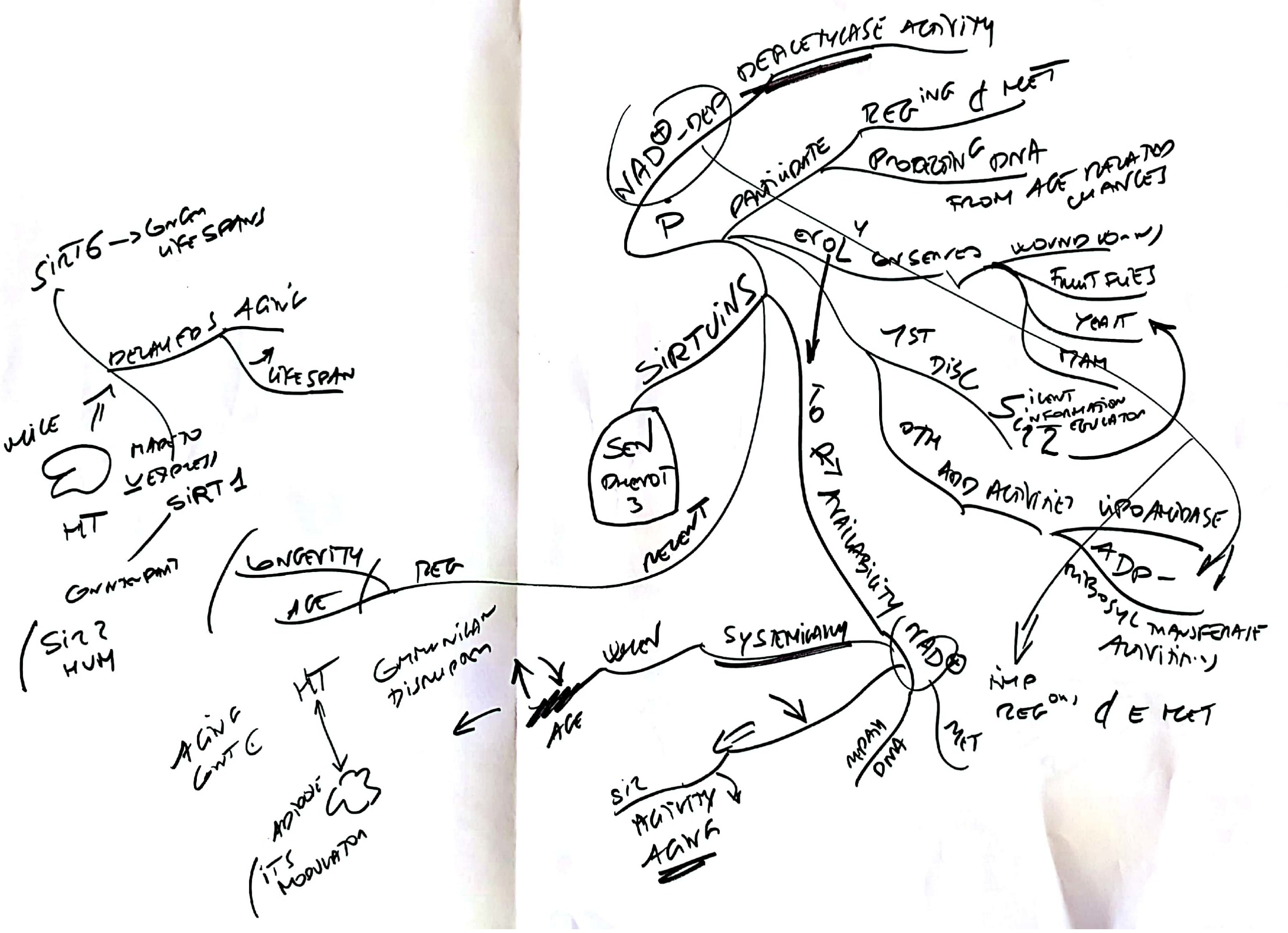


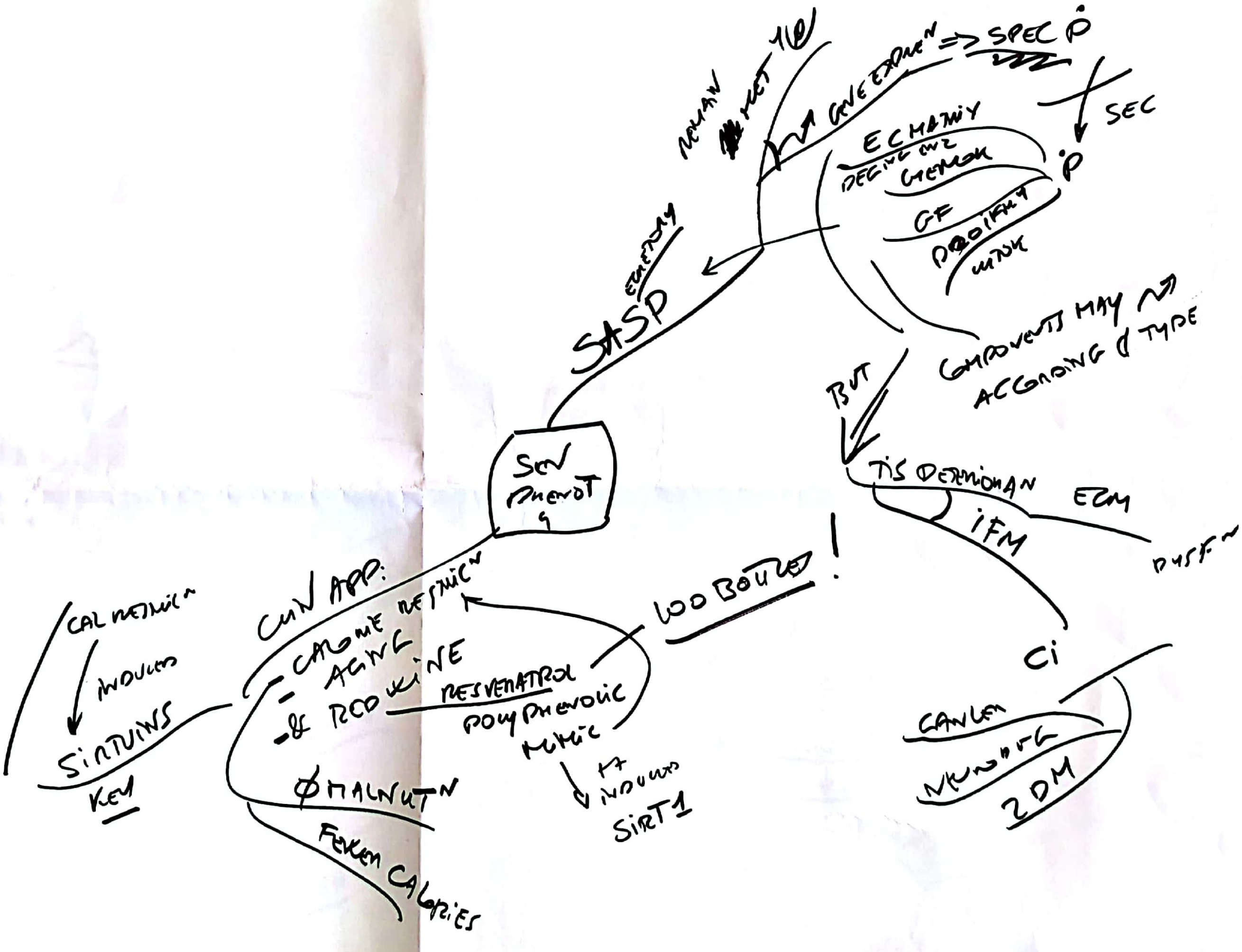
DYSFUNCTIONAL TELOMERES
STRONG MITOGENIC SIGNALS
CHROMATIN PERTURBATION & OTH STRESSES
DNA DAM
PRE-SEN ¢
SEN PHENOT
QUIESCENT
RESTING
SENESCENT PHENOTYPE
GARRETT
SA-B-GALACTOSIDASE
TERMINALLY DIFFED
CANNOT BE
BY PHYSIO
INCAP REPLICATION
GEN VIABLE
SURVIVE
LT
MET ACTIVE
ALSO EXPRESS
SA-B-gal
ENZ ACTIVITY
CDKi
INH CDK
STATE
INV G1
E2F
TF
CYCLINS
EXPREN
REGULATORS
AGING
IRREV

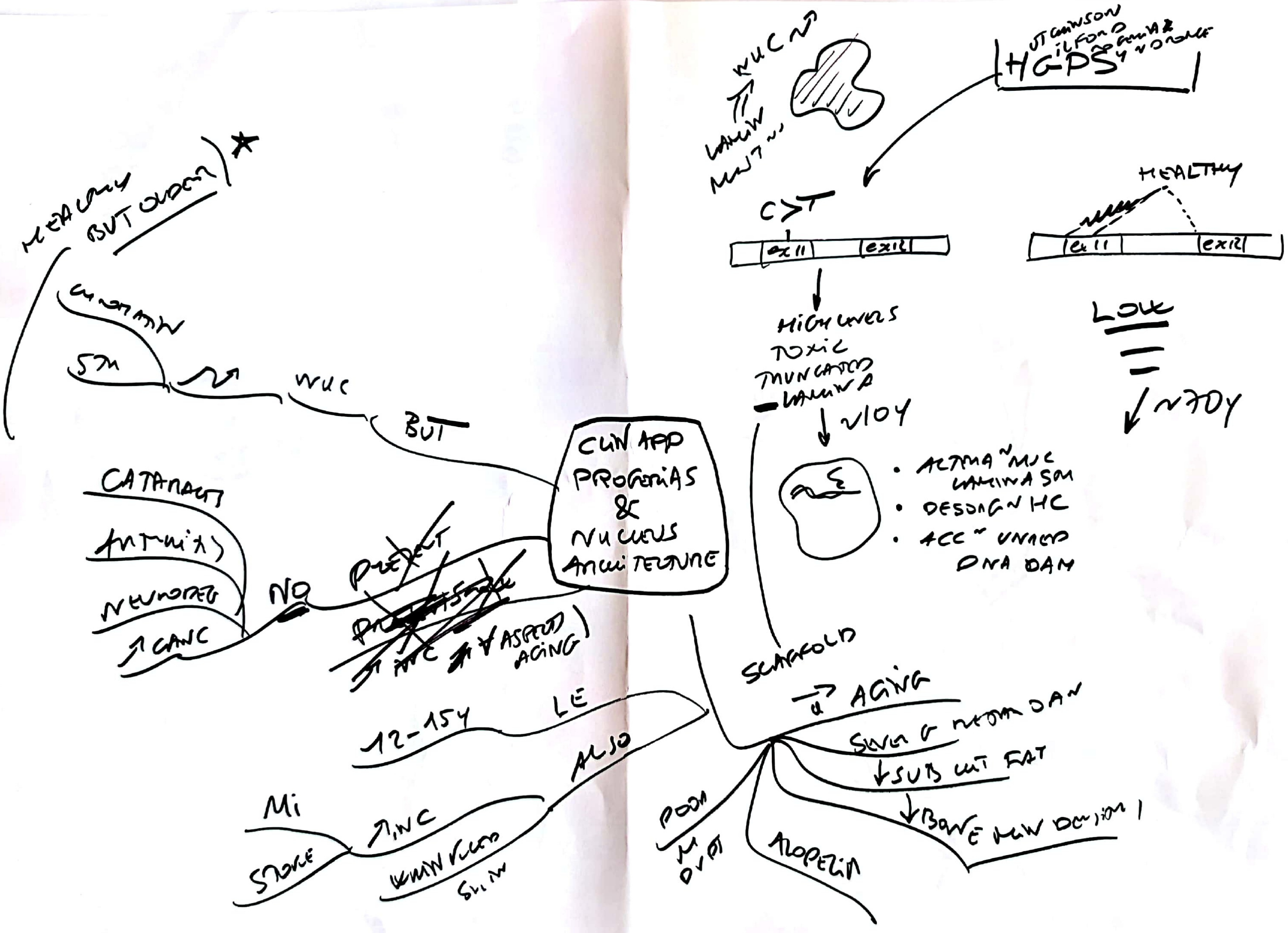


SEN-ASSOCIATED PROLIFN AI

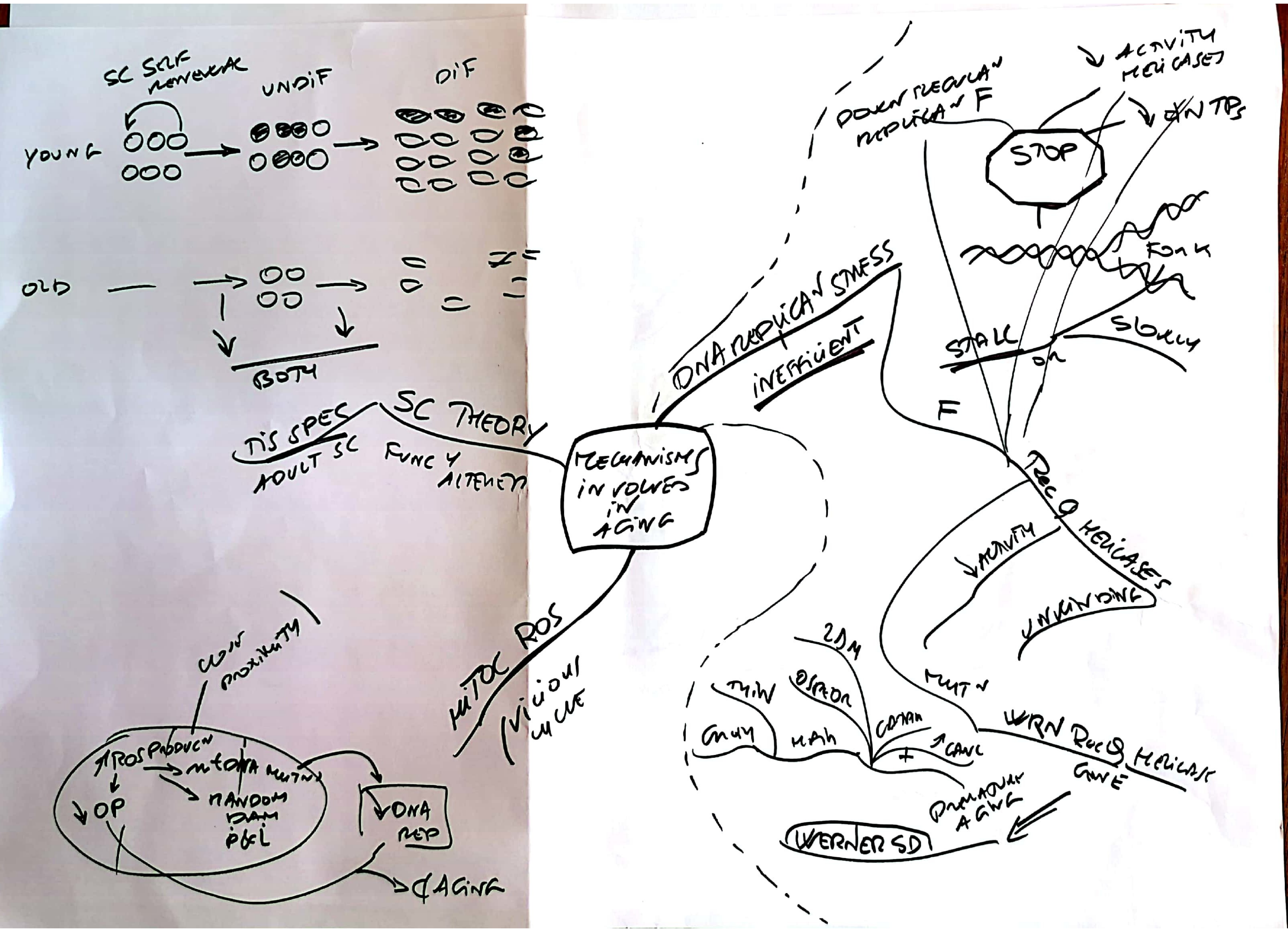


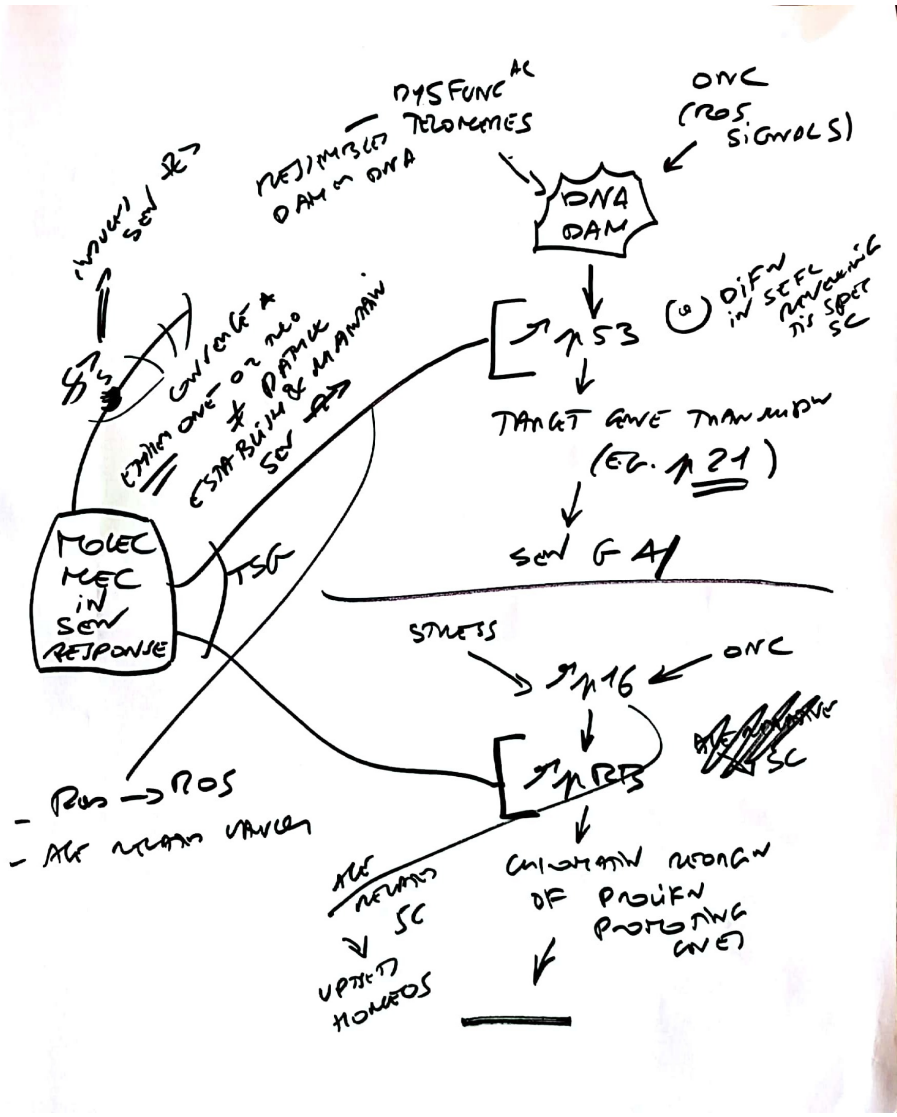

DEACETYLASE ACTIVITY
NAD+ DEP
P
PARTICIPATE
REG & MET
PROTECTING DNA
FROM AGE RELATED CHANGES
EVOL
CONSERVED
FRUIT FLIES
YEAST
1ST
DISC
SILENT INFORMATION REGULATOR
2
SIRTUINS
SEN
3
LIPOAMIDASE
ADP-
RIBOSYL TRANSFERASE
IMP
REG
& E MET
TO
NAD+
AVAILABILITY
SYSTEMICALLY
WHEN
AGE
SIR
ACTIVITY
AGING
DNA
MET
LONGEVITY
AGE
REG
SIRT6
LIFESPANS
AGING
LIFESPAN
MICE
HT
SIRT1
HUM
ADIPOSE
ITS
MODULATOR


SPEC P
SEC
P
SASP
BUT
COMPONENTS MAY
ACCORDING TYPE
ECM
IFM
Ci
CANCER
2DM
CLIN APP:
RESVERATROL
POLYPHENOLIC
INDUCES
SIRT1
SIRTUINS
KEY
FEWER CALORIES



CLIN APP
PROGERIAS
&
NUCLEUS
ARCHITECTURE
HUTCHINSON
GILFORD
HGPS
C>T
ex11
ex12
HIGH LEVELS
TOXIC
TRUNCATED
LAMINA
↓10Y
HEALTHY
LOW
↓70Y
DESIGN HC
DNA DAM
BUT
CATARACT
NO
AGING
12-15Y
LE
ALSO
MI
STROKE
SKIN
ALOPECIA
SCAFFOLD
↓SUB CUT FAT


MECHANISMS INVOLVED IN AGING
SC THEORY
TIS SPEC ADULT SC
FUNC ALTERATION
SC SELF RENEWAL
UNDIF
DIF
YOUNG
OLD
BOTH
MITOC ROS
VICIOUS CYCLE
↑ROS PRODUCN
MTDNA MUTN
RANDOM DAM
↓OP
DNA REP
AGING
DNA REPLICAN STRESS
INEFFICIENT
DOWN REGULAN REPLICAN F
↓ ACTIVITY HELICASES
↓ DNTPS
STOP
FORK
STALL
SLOWLY
OR
F
RecQ HELICASES
↓ ACTIVITY
UNWINDING
MUTN
WRN RecQ HELICASE GENE
PREMATURE AGING
WERNER SD
T2DM
THIN
OSTEOP
CATAR
GRAY
HAIR
CANC


DYSFUNC AL TELOMERES
ONC (ROS SIGNALS)
DNA DAM
p53
TARGET GENE TRANSCRIPTION
(EG. p21)
SEN GA
MOLEC MEC IN SEN RESPONSE
TSG
STRESS
p16
ONC
pRB
SC
CHROMATIN REORGAN OF PROLIFN PROMOTING GENES
UPREG HOMEOS