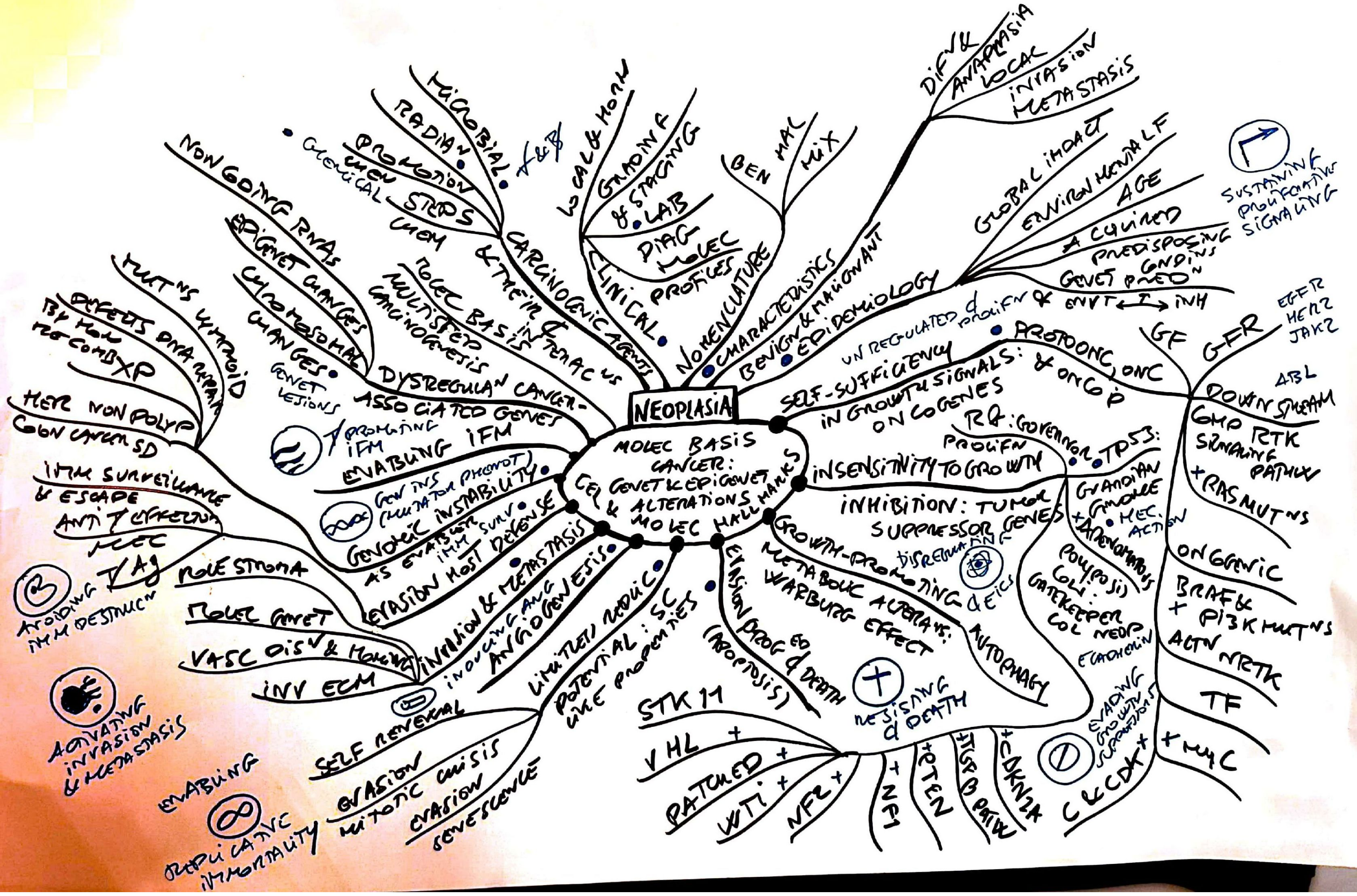
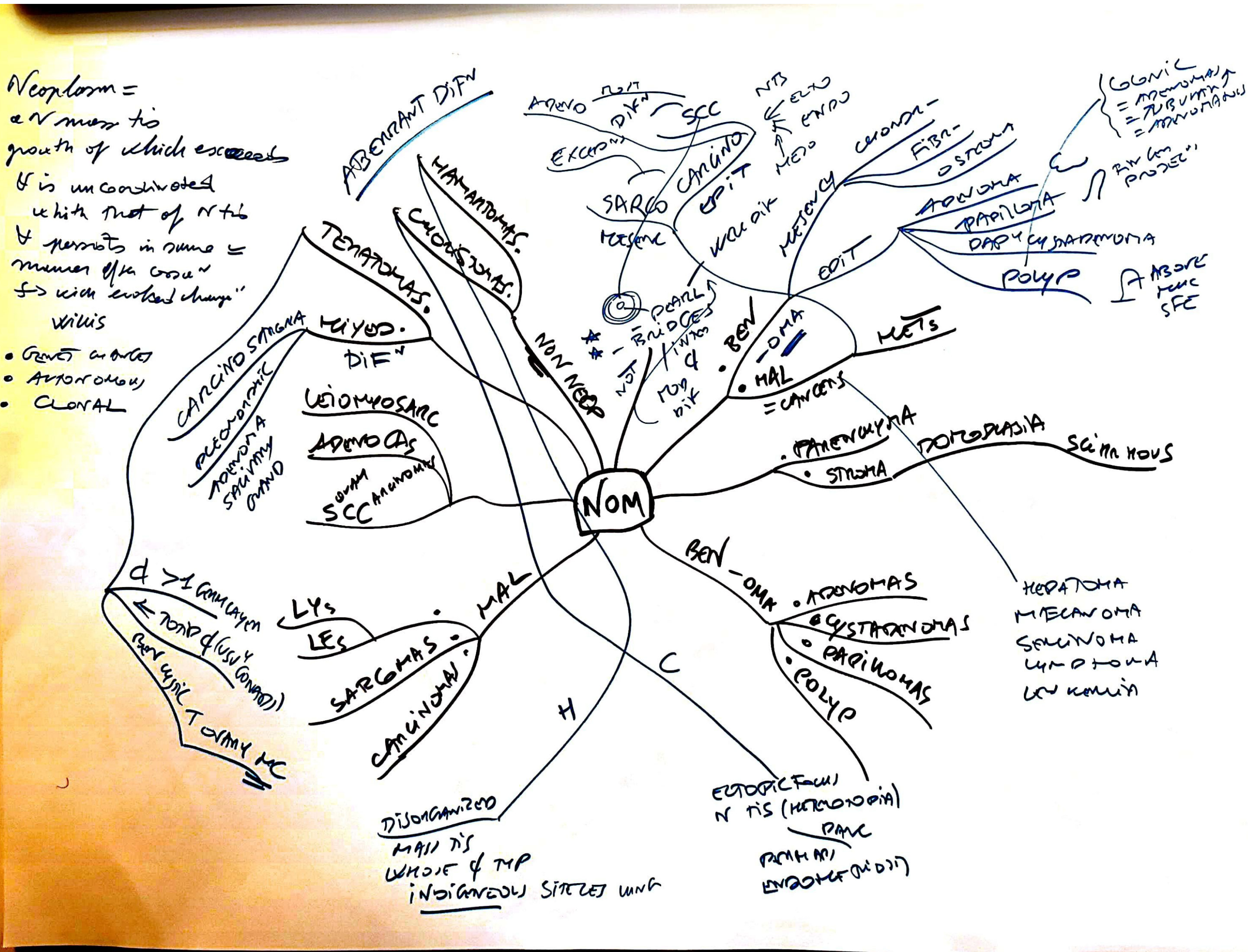
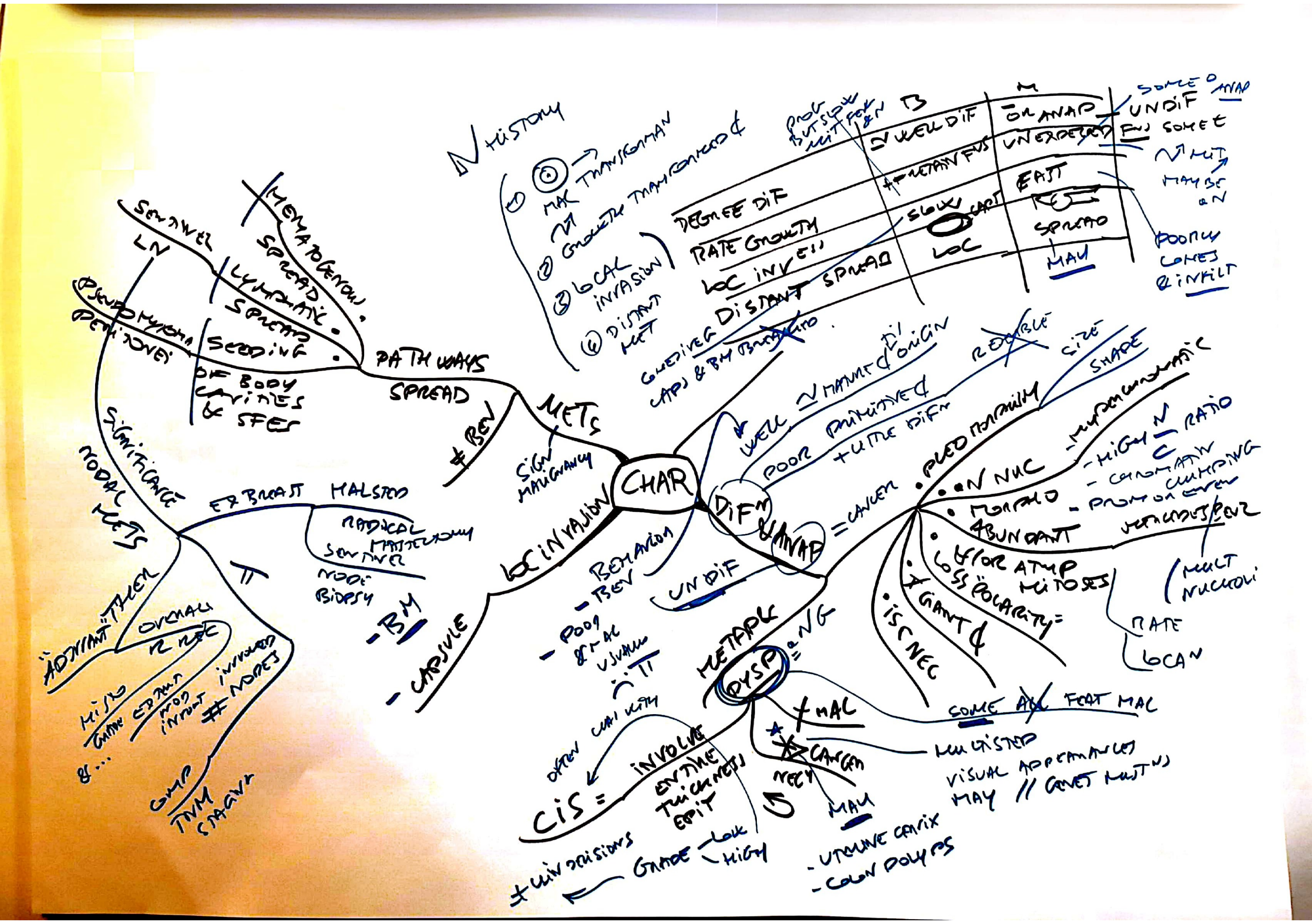
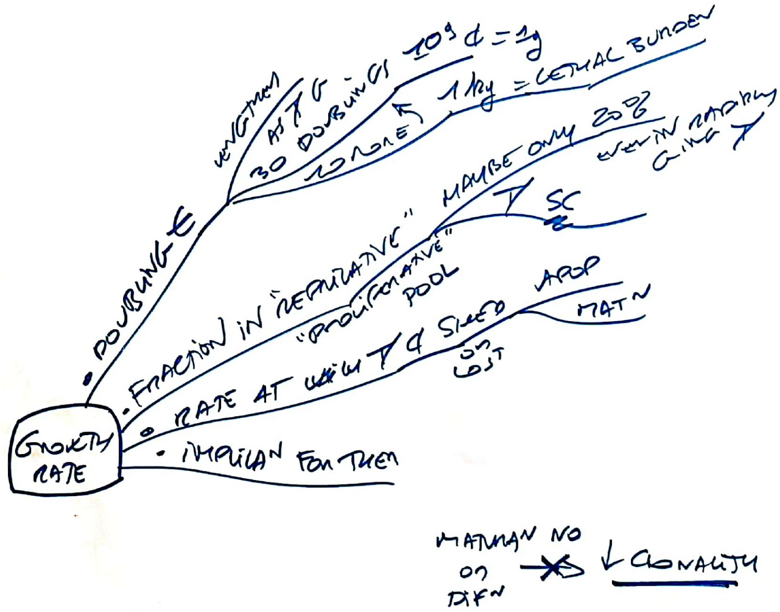

NEOPLASIA
MOLEC BASIS CANCER: CEL GENET & EPIGENET ALTERATIONS & MOLEC HALLMARKS
SELF-SUFFICIENCY IN GROWTH SIGNALS: ONCOGENES
UNREGULATED PROLIFN
PROTOONC, ONC & ONCOP
GF
GFR
EGFR
HER2
JAK2
ABL
DOWNSTREAM
CMP RTK SIGNALING PATHW
RAS MUTns
ONCOGENIC
BRAF & PI3K MUTns
ACTV NRTK
TF
MYC
CKCDK
SUSTAINING PROLIFERATIVE SIGNALING
INSENSITIVITY TO GROWTH INHIBITION: TUMOR SUPPRESSOR GENES
RB: GOVERNOR PROLIFN
TP53: GUARDIAN GENOME
MEC. ACTION
ADENOMATOUS POLYPOSI COLI: GATEKEEPER COL NEOP
E CADHERIN
CDKN2A
TGFB PATHW
PTEN
NF1
NF2
WT1
PATCHED
VHL
STK11
EVADING GROWTH SUPPRESSORS
GROWTH-PROMOTING METABOLIC ALTERATNS: WARBURG EFFECT
AUTOPHAGY
EVASION PROG ED CELL DEATH (APOPTOSIS)
RESISTING CELL DEATH
LIMITLESS REPLIC POTENTIAL: SC LIKE PROPERTIES
SELF RENEWAL
EVASION MITOTIC CRISIS
EVASION SENESCENCE
ENABLING
REPLICATIVE IMMORTALITY
INDUCING ANGIOGENESIS
INVASION & METASTASIS
INV ECM
VASC DISSEM & HOMING
MOLEC GENET
ROLE STROMA
ACTIVATING INVASION & METASTASIS
EVASION HOST DEFENSE AS EVASION IMM SURV
IMM SURVEILLANCE & ESCAPE
ANTI T EFFECTOR MEC
Ag
AVOIDING IMM DESTRUCTION
GENOMIC INSTABILITY
GEN INS (MUTATOR PHENOT)
HER NONPOLYP COLON CANCER SD
DEFECTS DNA REPAIR BY HOM RECOMB
XP
MUTns LYMPHOID
ENABLING IFM
PROMOTING IFM
DYSREGULAR CANCER-ASSOCIATED GENES
GENET LESIONS
CHROMOSOMAL CHANGES
EPIGENET CHANGES
NONCODING RNAs
MOLEC BASIS MULTISTEP CARCINOGENESIS
CARCINOGENIC AGENTS & THEIR CEL INTERAC
STEPS
CHEM
PROMOTION
CHEMICAL
RADIAN
MICROBIAL
CLINICAL
LOCAL & HORM
GRADING & STAGING
LAB
DIAG MOLEC PROFILES
NOMENCLATURE
BEN
MAL
MIX
CHARACTERISTICS BENIGN & MALIGNANT
DIFN & ANAPLASIA
LOCAL INVASION
METASTASIS
EPIDEMIOLOGY
GLOBAL IMPACT
ENVIRONMENTAL F
AGE
ACQUIRED PREDISPOSING CONDITIONS
GENET PREDN
ENVT ↔ INH

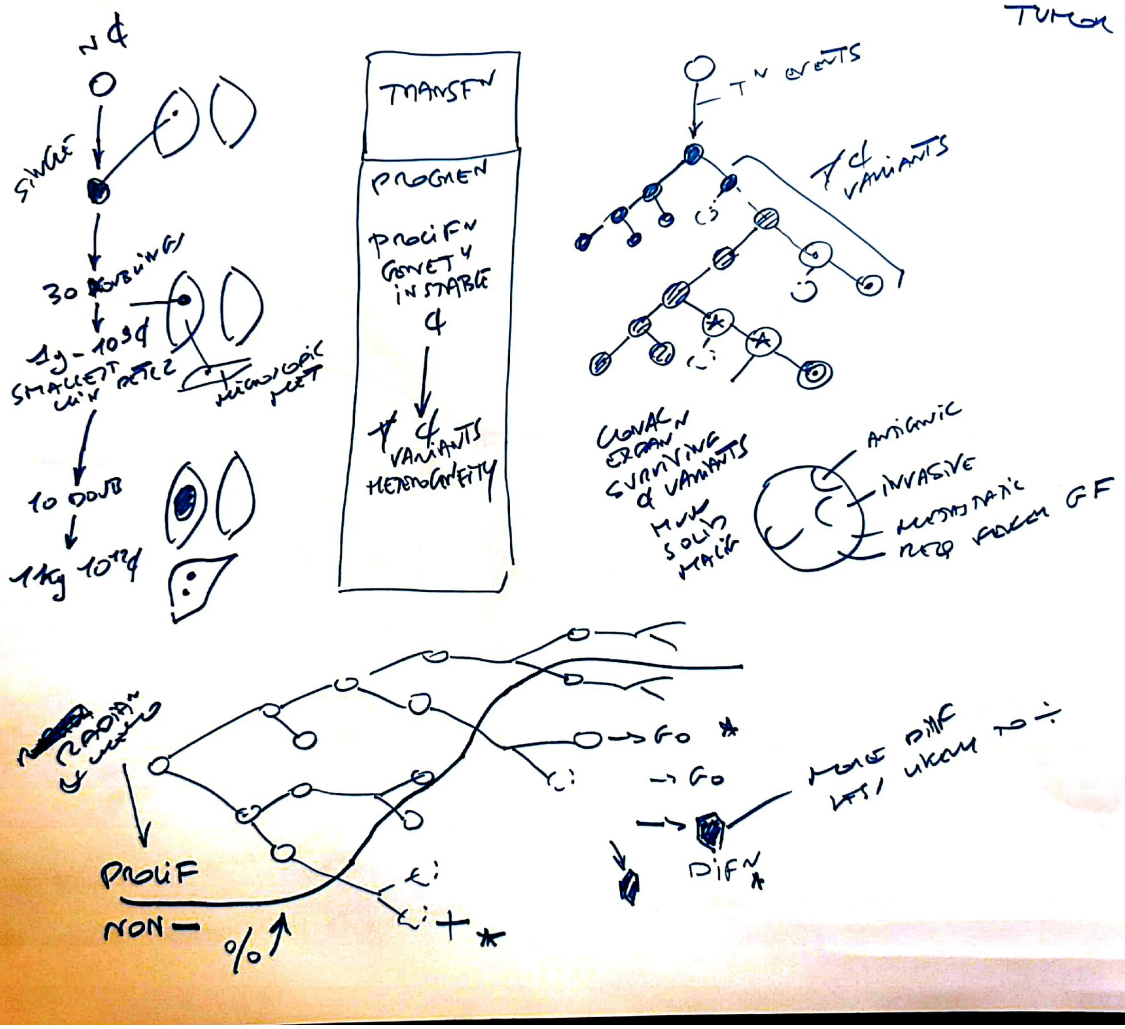


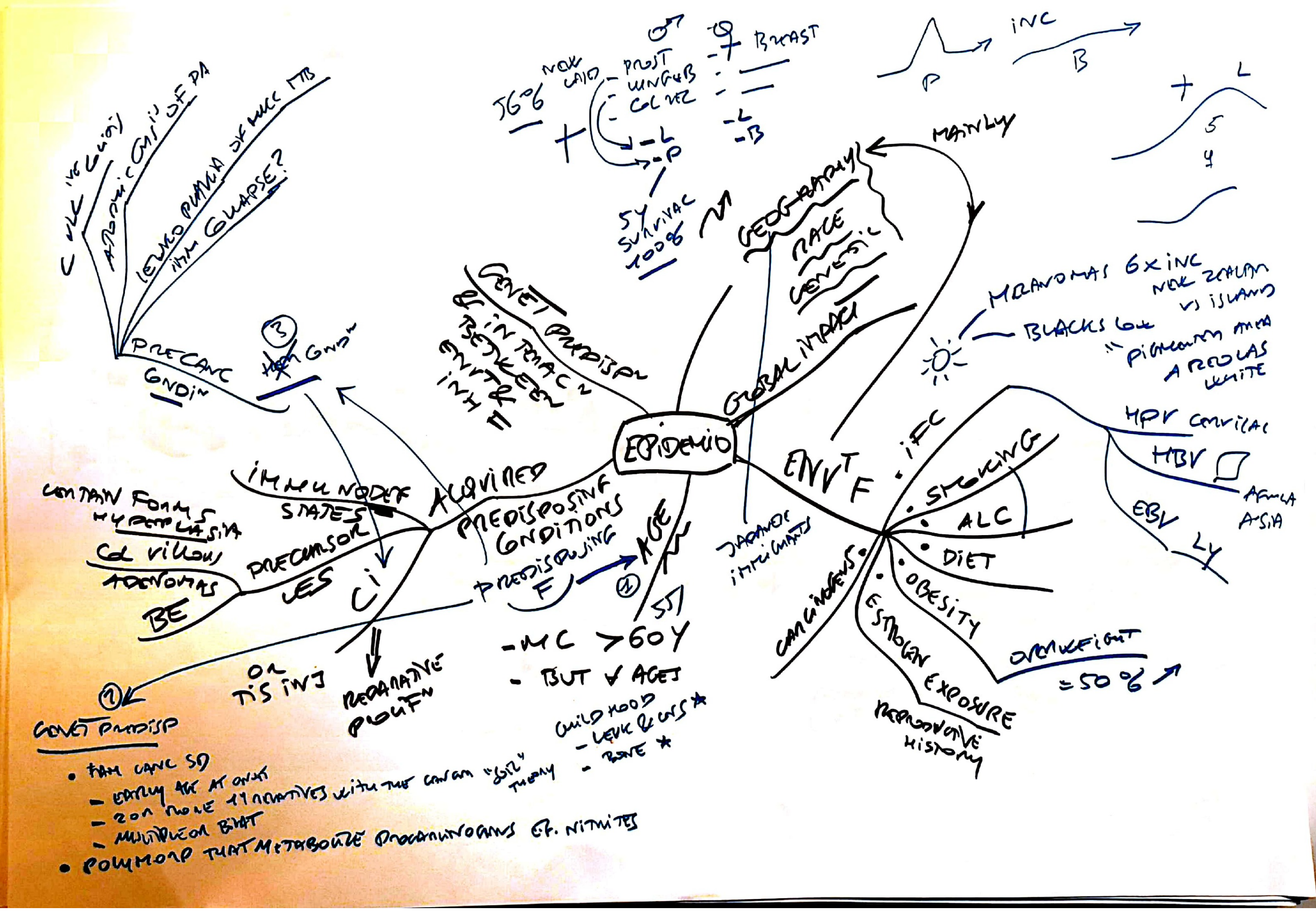
Neoplasm =
a N mass tis
growth of which exceeds
& is uncoordinated
with that of N tis
& persists in same
manner after cessation
of stimuli which evoked change
Willis
• Genet changes
• Autonomous
• Clonal
ABERRANT DIFN
HAMARTOMAS.
CHORISTOMAS.
TERATOMAS.
MIXED.
DIFN
CARCINOSARCOMA
PLEOMORPHIC ADENOMA SALIVARY GLAND
LEIOMYOSARC
ADENOCAS
SCC
NON NEOP
NOM
SARCO
CARCINO
SCC
MESENCH
EPIT
PEARLS
BRIDGES
NOT WELL DIF
WELL DIF
MOD DIF
BEN
MAL
-OMA
METS
= CANCERS
MESENCH
EPIT
CHONDR-
FIBR-
OSTEOMA
ADENOMA
PAPILLOMA
POLYP
STROMA
DESMOPLASIA
SCIRRHOUS
HEPATOMA
MELANOMA
SEMINOMA
LYMPHOMA
LEUKEMIA
BEN -OMA
• ADENOMAS
• CYSTADENOMAS
• PAPILLOMAS
• POLYP
MAL
SARCOMAS
CARCINOMAS
LYs
LEs
H
C
DISORGANIZED
MAIN TIS
WHOLE & TYP
INDIGENOUS
ECTOPIC FOCI
N TIS (HETEROTOPIA)


CHAR
METS
SIGN MALIGNANCY
LOC INVASION
DIFN
UNANAP
PATHWAYS SPREAD
HEMATOGENOUS SPREAD
LYMPHATIC SPREAD
SEEDING OF BODY CAVITIES & SFCES
SENTINEL LN
SIGNIFICANCE NODAL METS
EX BREAST HALSTED
RADICAL MASTECTOMY
SENTINEL NODE BIOPSY
ADJUVANT THER
OVERALL
TNM STAGING
- BM
- CAPSULE
BEHAVIOR
- BEV
UNDIF
WELL
POOR
SIZE
SHAPE
PLEOMORPHISM
N NUC
HYPERCHROMATIC
MORPHO
ABUNDANT
ATYP MITOSES
LOSS POLARITY
GIANT ¢
ISC NEC
MULT NUCLEOLI
RATE
LOCAN
METAPL
DYSP
MAL
CANCER
NEC
MAL
- UTERINE CERVIX
- COLON POLYPS
CIS = INVOLVE ENTIRE THICKNESS EPIT
GRADE - LOW - HIGH
SOME AX FEAT MAL
N HISTORY
DEGREE DIF
RATE GROWTH
LOC INV
DISTANT SPREAD
B
M
WELL DIF
UNDIF
SLOW
FAST
LOC
SPREAD
MAL


GROWTH RATE
• DOUBLING T
30 DOUBLINGS 10^9 ¢ = 1g
1 kg = LETHAL BURDEN
• FRACTION IN "REPLICATIVE" "PROLIFERATIVE" POOL
MAYBE ONLY 20%
SC
• RATE AT WHICH ¢ SHED
APOP
MATN
or LOST

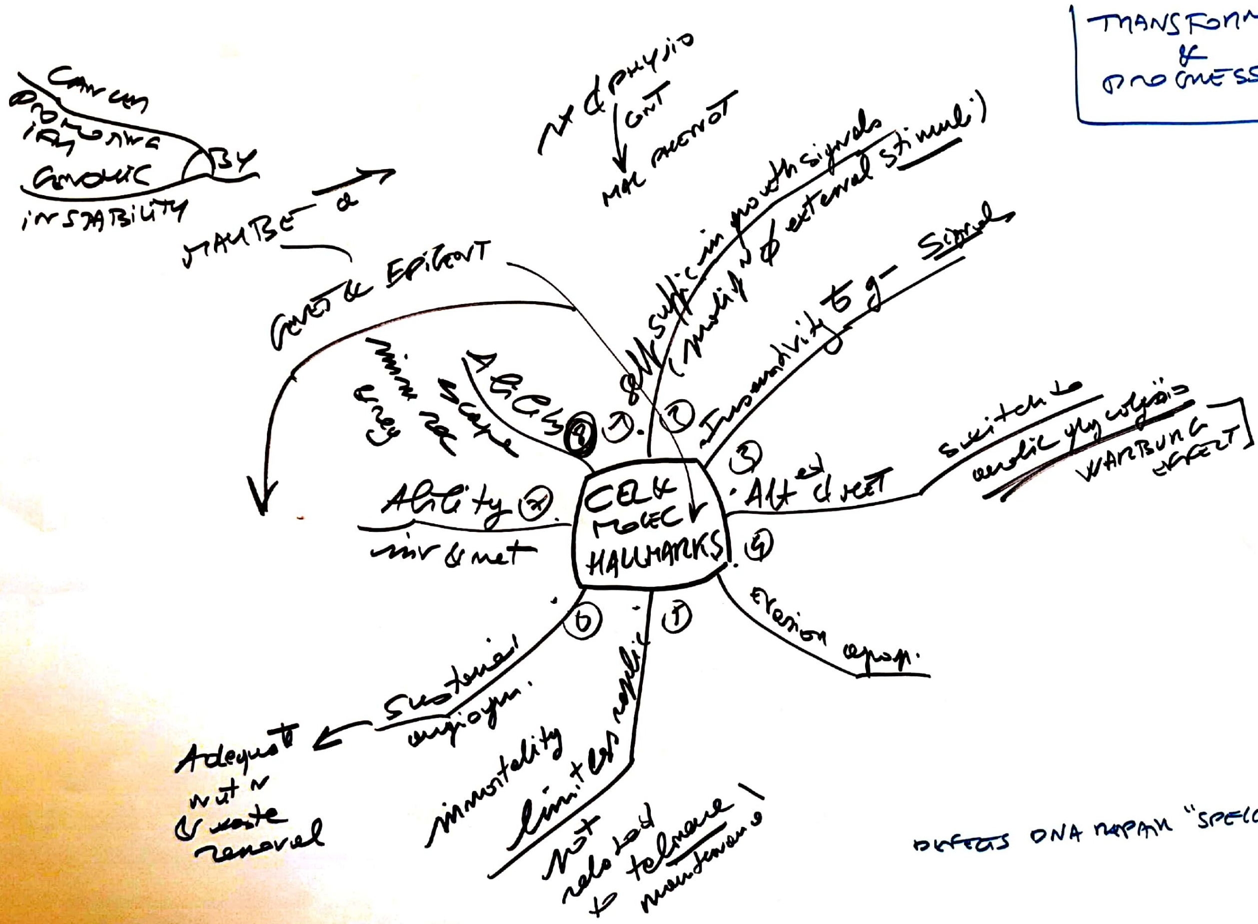
Biology
Tumor Growth



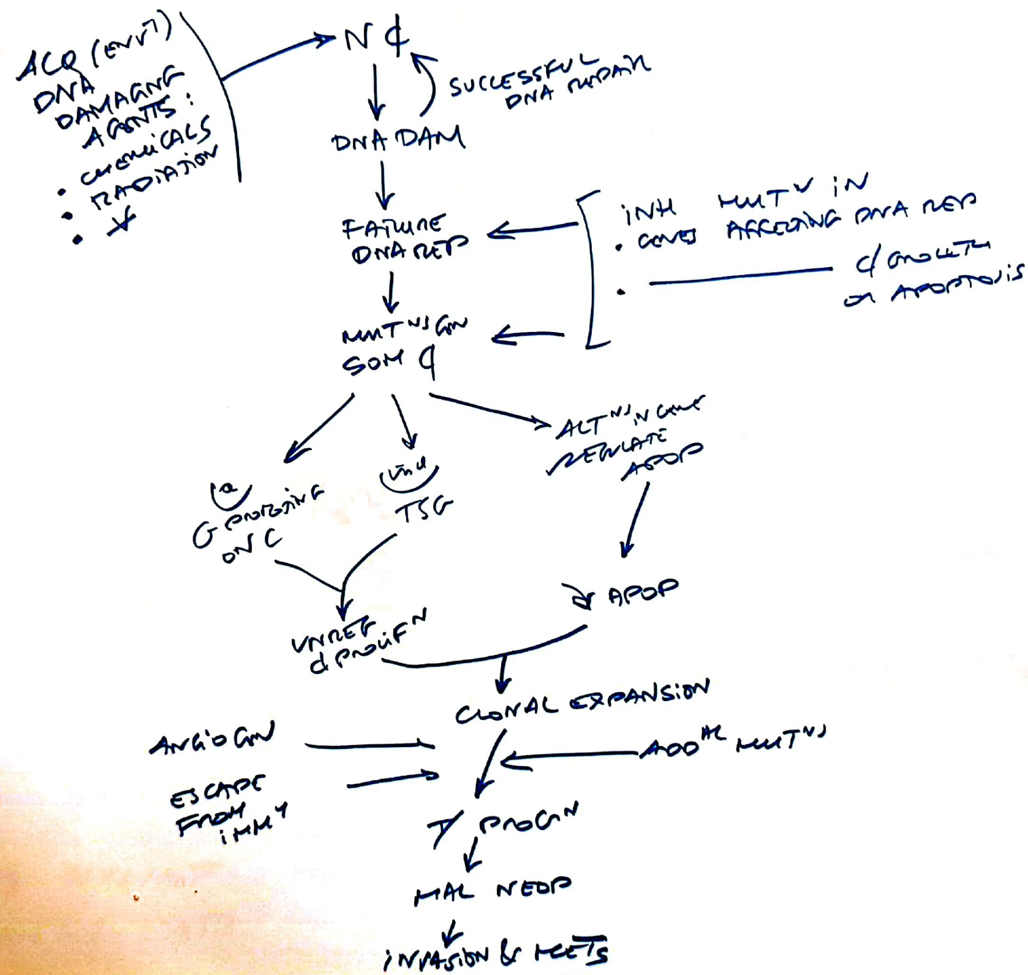

EPIDEMIO
GENET PREDISP
& INTERAC BETWEEN ENVT & INH F
GEOGRAPHY
RACE
GENETIC
GLOBAL IMPACT
MAINLY
ENVT F
SMOKING
ALC
DIET
OBESITY
OVERWEIGHT
≈50%
ESTROGEN EXPOSURE
REPRODUCTIVE HISTORY
CARCINOGENS
MELANOMAS 6x INC
NEW ZEALAND vs ISLAND
BLACKS LOW
PIGMENTED AREA
AREOLAS WHITE
HPV CERVICAL
HBV
AFRICA ASIA
EBV
LY
JAPANESE IMMIGRANTS
AGE
5Y
-MC >60Y
- BUT ∀ AGES
CHILDHOOD
- LEUKAEMIAS
- BONE
PREDISPOSING F
ACQUIRED PREDISPOSING CONDITIONS
IMMUNODEF STATES
PRECURSOR LES
CI
REPARATIVE PROLIFN
OR TIS INJ
CONTAIN FORMS HYPERPLASIA
Col villous
ADENOMAS
BE
PRECANC CONDIN
GENET PREDISP
• FAM CANC SD
- EARLY AGE AT ONSET
- 2 OR MORE RELATIVES WITH THE CANCER
- MULTIPLE OR BILAT
• POLYMORP THAT METABOLIZE PROCARCINOGENS EG. NITRITES
56%
NEW CANC
PROST
LUNG+B
COLREC
BREAST
5Y SURVIVAL
INC
B
L

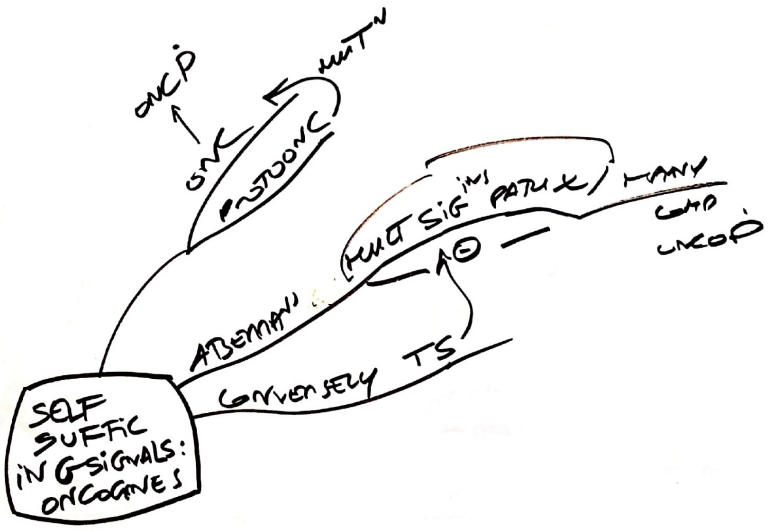

MOLEC BASIS: ROLE GENET & EPIGENET
"USUAL" SUSPECTS
MONOCLONAL
UNDERLIES CARCINOGENESIS
A tumor is formed by clonal expansion of a single prec cell that has incurred genet damage (i.e clonal)
4 CLAS ✓ REG GENES
G ⊕ PROTOONC
G ⊖ TSG
REG APOP
REG DNA REPAIR
MUTATOR PHENOT
⊙ MUT'N
results from accumulation of complementary mut'ns in a stepwise fashion
CANCER HALLMARKS
PHENOTYP ATTRIBUTES
PROGRESSION
MULTI STEP PROCESS
INITIATING DRIVER MUTN
MUTATIONS ≠ PASSENGER
Common early step sporadic & social
LOF MUT'N
EPIGENETIC ALSO
DNA MUT'N
explain history & RT following therapy
once established, tumors evolve genet'y during their outgrowth & progression under the pressure of Darwinian selection

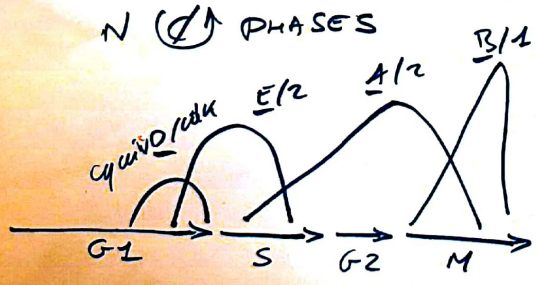
TRANSFORMATION & PROGRESSION



DEFECTS DNA REPAIR "SPELL CHECKER"


ACQ (ENVT) DNA DAMAGING AGENTS:
• CHEMICALS
• RADIATION
• V
N ¢
SUCCESSFUL DNA REPAIR
DNA DAM
FAILURE DNA REP
INH MUTN IN
• GENES AFFECTING DNA REP
• ¢ GROWTH OR APOPTOSIS
MUTNS GN SOM ¢
ALTNS IN GENES REGULATE APOP
¢ GROWTH PROMOTING ONC
TSG
UNREG ¢ PROLIFN
↓ APOP
CLONAL EXPANSION
ANGIOGN
ESCAPE FROM IMMY
ADDNL MUTNS
T PROGN
MAL NEOP
INVASION & METS





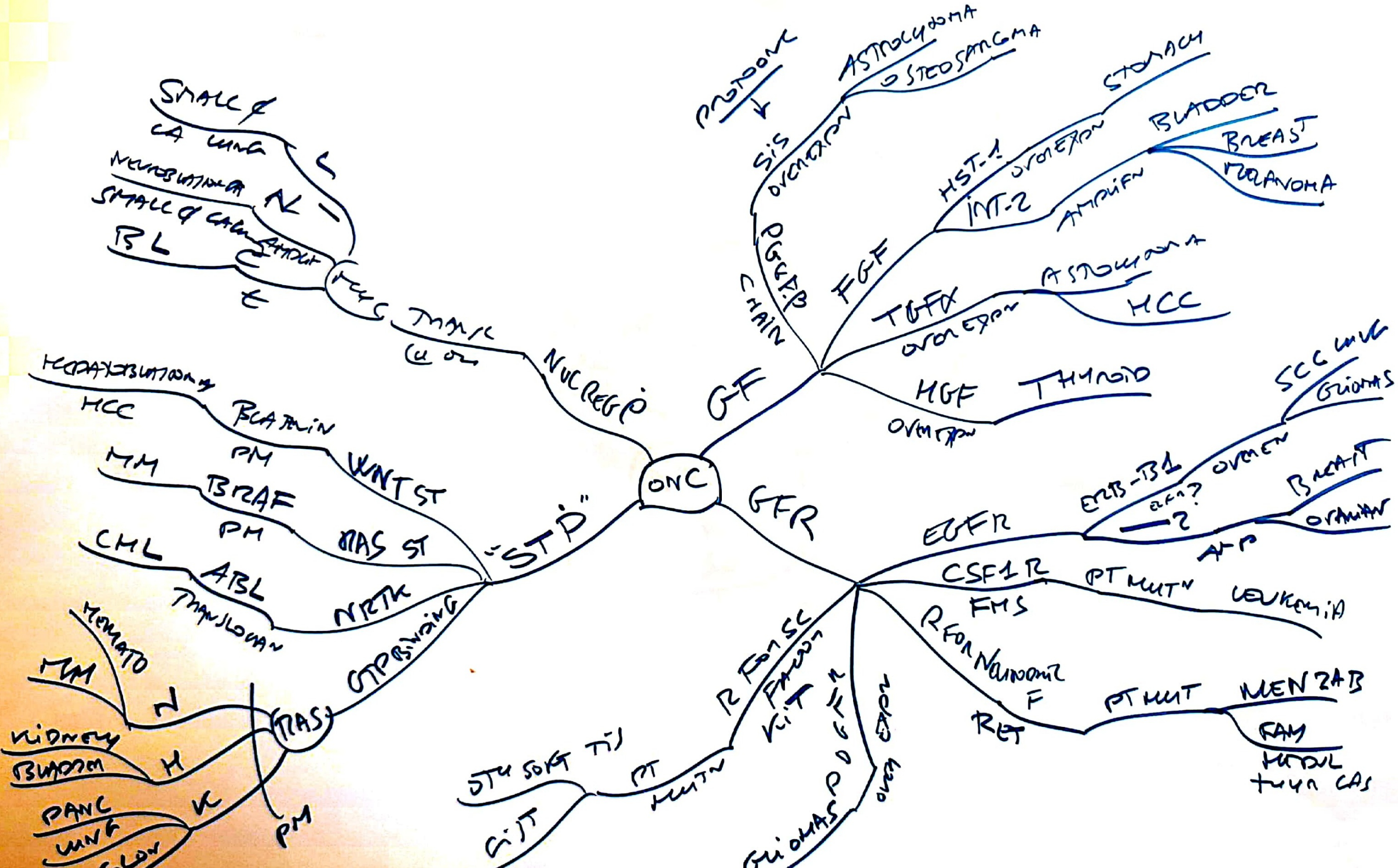
CDK ENZ — (P) — Ṗ IN ORDER NEXT PHASE CA

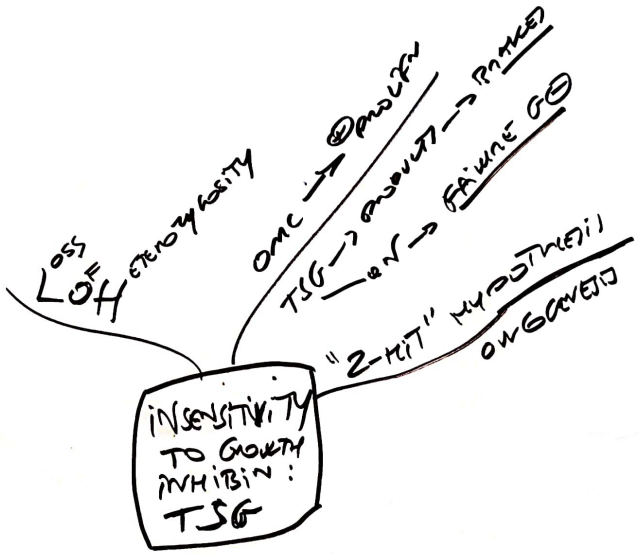
"REG" MEANS "GNT" MEANS "SUP"

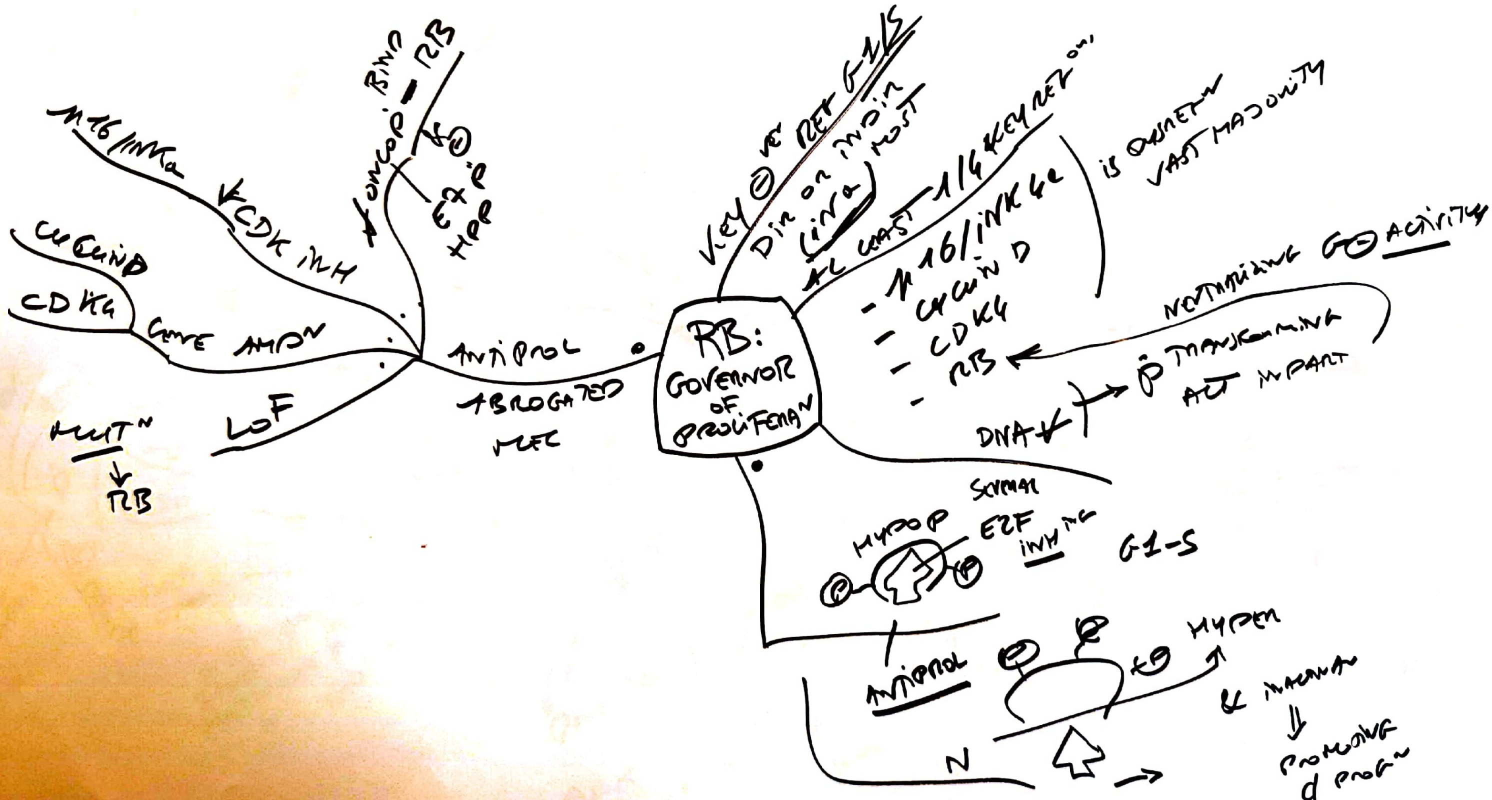
INTERN: CYCLIN/CDK INK4/ANF

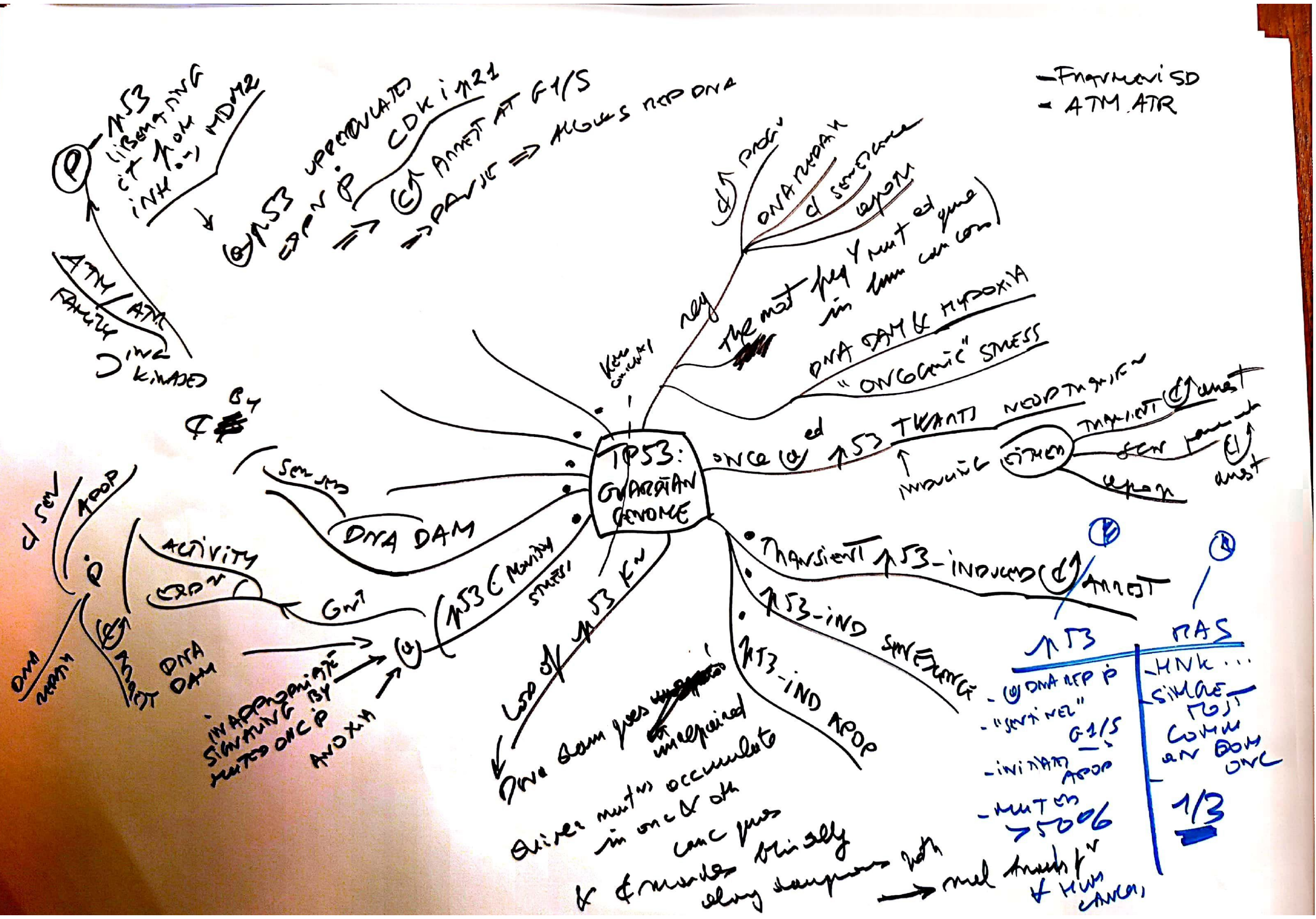
T (REALLY KNOWN) SG: P53


PROTO ONC ONC & ONC P
MYC
TF
ALSO APOP
CDK
G1/S G2/M checkpoints
GOF
LOF TSG
G1/S
DK CDD4
REGULATIONS
GF
GFR
AUTOC
EGF RTK
ERBB1
ERBB2
LIGAND
HER2 RTK
GENE AMPLIFN
JAK2 TK
ABL NRTK
BCR-ABL
CML
ALLE
DOWNSTREAM COMP
RTK SIGNALING PATHWAYS
STP (RAS)
GP
RAS MUTNS
MANY
ONCOGENIC BRAF & PI3K MUTNS
BRAF
PI3K FAM
MASTER TF
some context
up-regulates telomerase
genes involved
NUC REG P
PROTO ONC
ONC
MUT OR OVEREXPRESSED

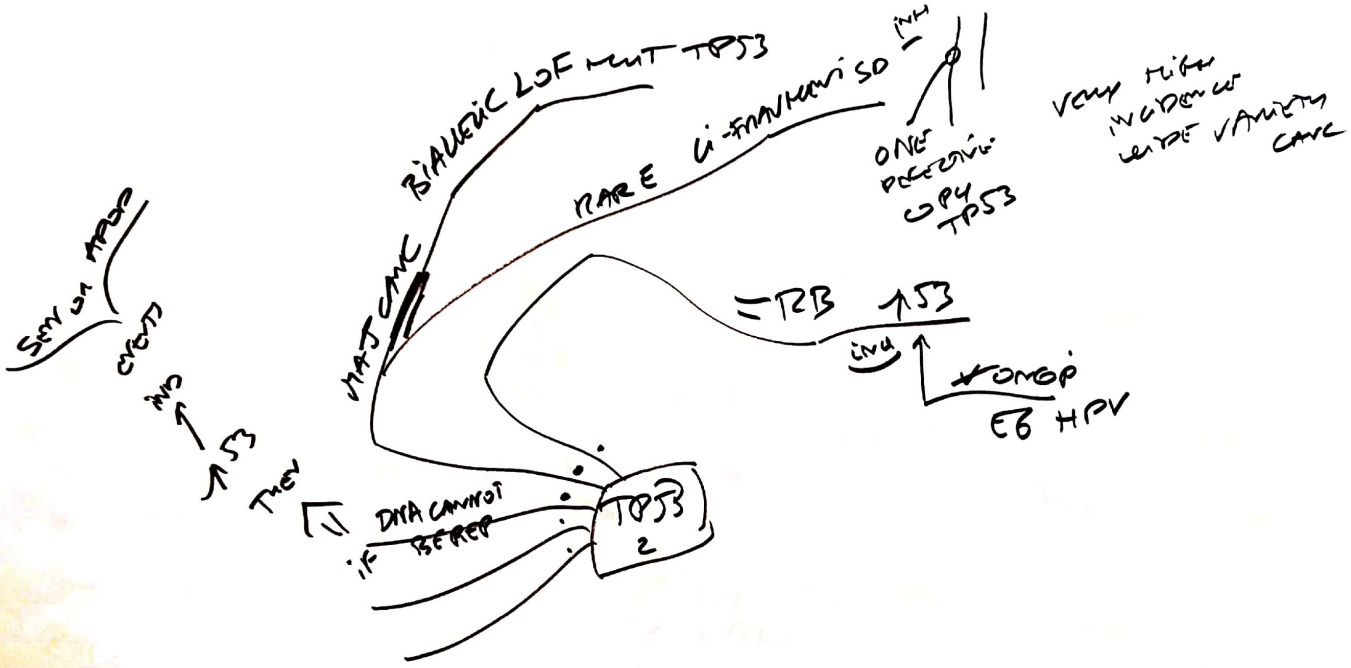

ONC
GF
GFR
"STP"
NUC REG P
PROTOONC
SIS
ASTROCYTOMA
OSTEOSARCOMA
OVEREXPN
PDGF-B CHAIN
FGF
HST-1
INT-2
OVEREXPN
STOMACH
AMPLIFN
BLADDER
BREAST
MELANOMA
TGFα
ASTROCYTOMA
HCC
OVEREXPN
HGF
THYROID
OVEREXPN
EGFR
ERB-B1
OVEREXPN
SCC LUNG
GLIOMAS
?
AMP
BREAST
OVARIAN
CSF1R
FMS
PT MUTN
LEUKEMIA
R FOR NEUROTR F
RET
PT MUT
MEN 2A,B
FAM
MEDULL
THYR CAs
R FOR SC FACTOR
KIT
PT
MUTN
GIST
PDGFR
OVEREXPN
GLIOMAS
MYC
TRANSLOC
C
N
L
SMALL C CA LUNG
NEUROBLASTOMA
BL
HEPATOBLASTOMA
HCC
B-CATENIN
PM
WNT ST
MM
BRAF
PM
RAS ST
CML
ABL
TRANSLOCATION
NRTK
GTP BINDING
RAS
HEMATO
MM
N
KIDNEY
BLADDER
H
PANC
LUNG
COLON
K
PM

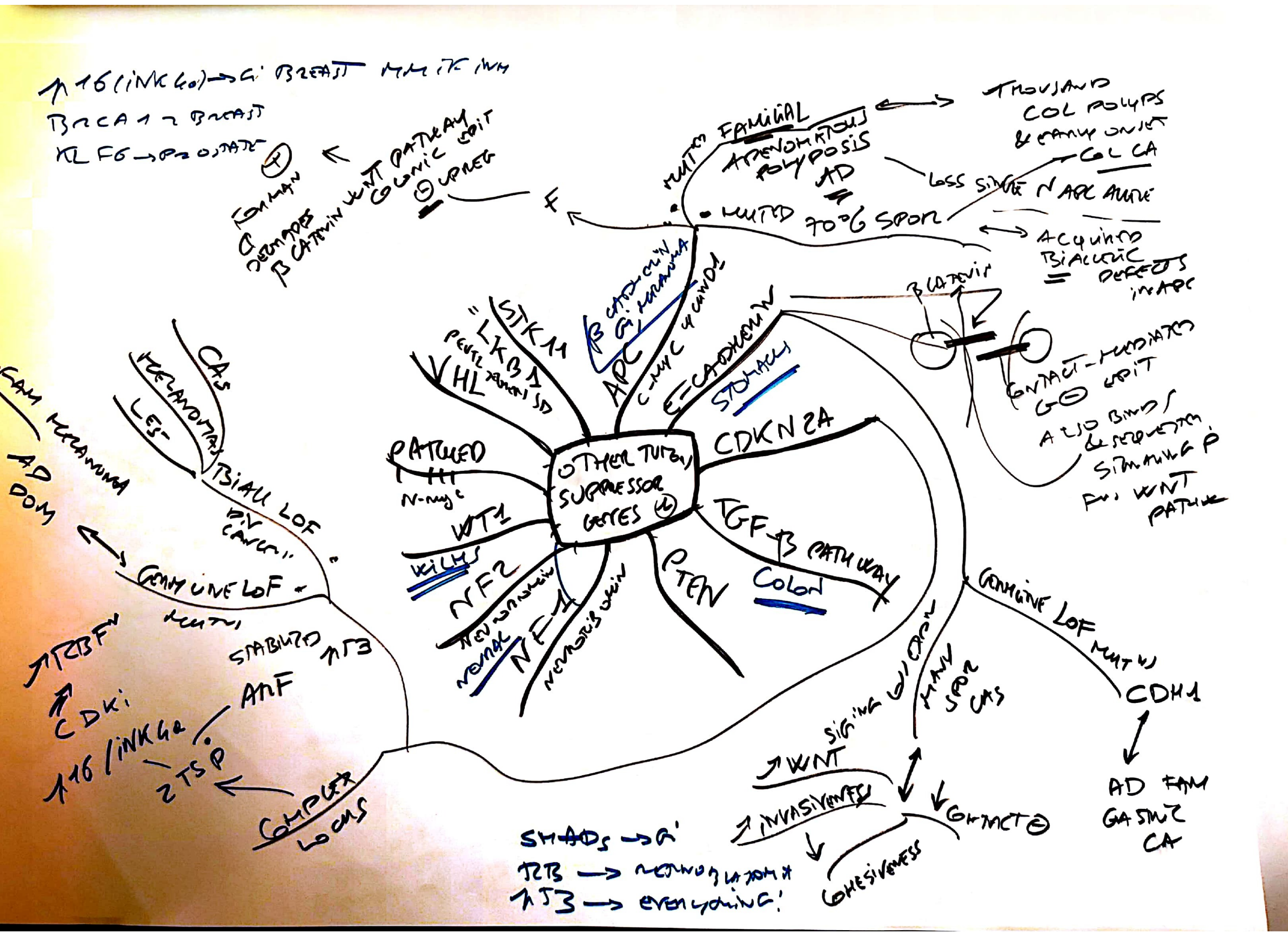

LOSS OF ETEROZYGOSITY
OMC → @PROLIFN
TSG → @SURVIVIN → PROMOTES GROWTH
"2-HIT" HYPOTHESIS
OVEREXPRESSED
INSENSITIVITY TO GROWTH INHIBITION: TSG


RB:
GOVERNOR
OF
PROLIFERAN
ANTIPROL
ABROGATED
CDK INH
GENE AMPN
CD K4
LOF
RB
SCYCLIN D
ANTIPROL
DNA
G1-S
HYPER
N
HYPOP
E2F
CDK4
CYCLIN D

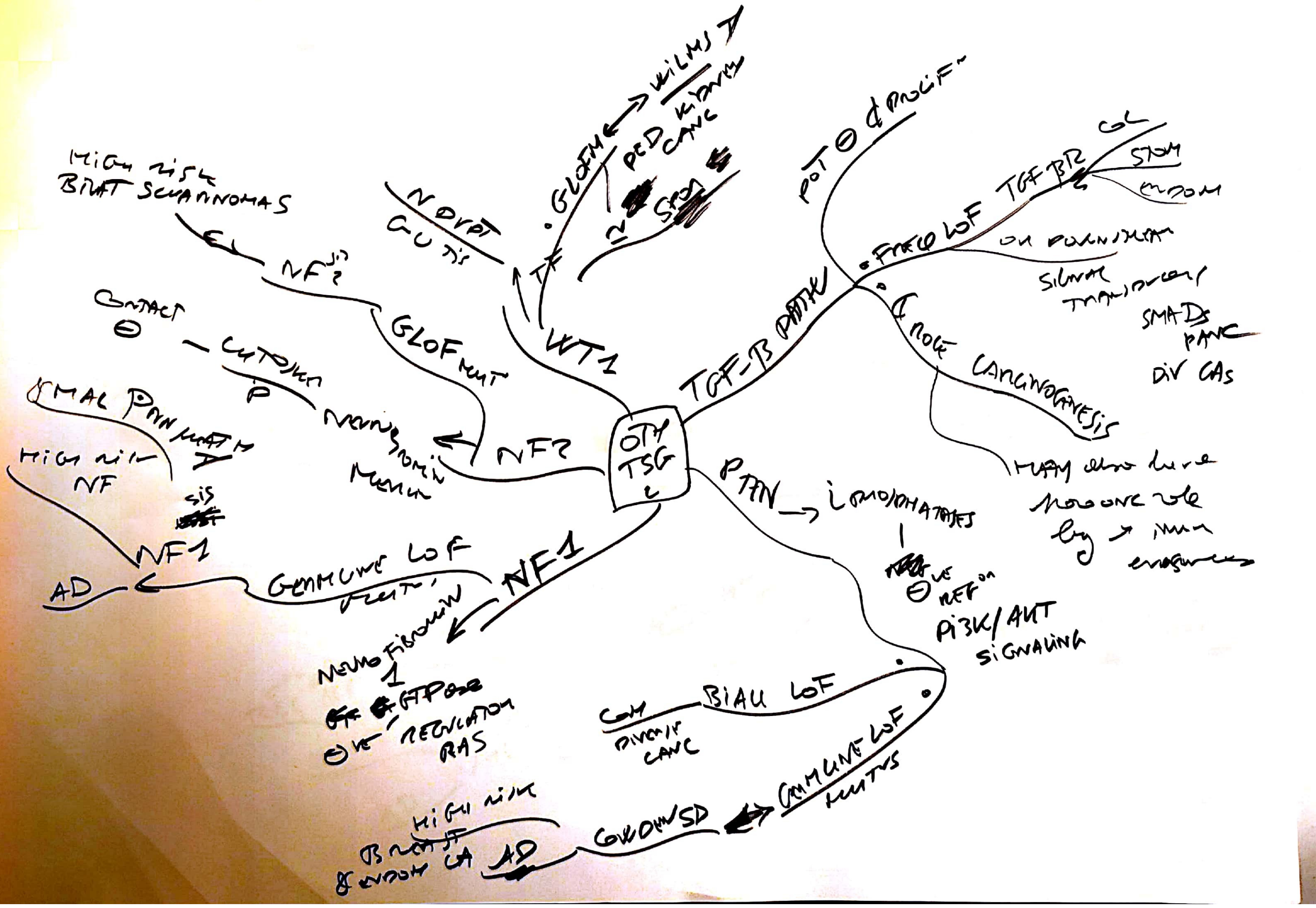


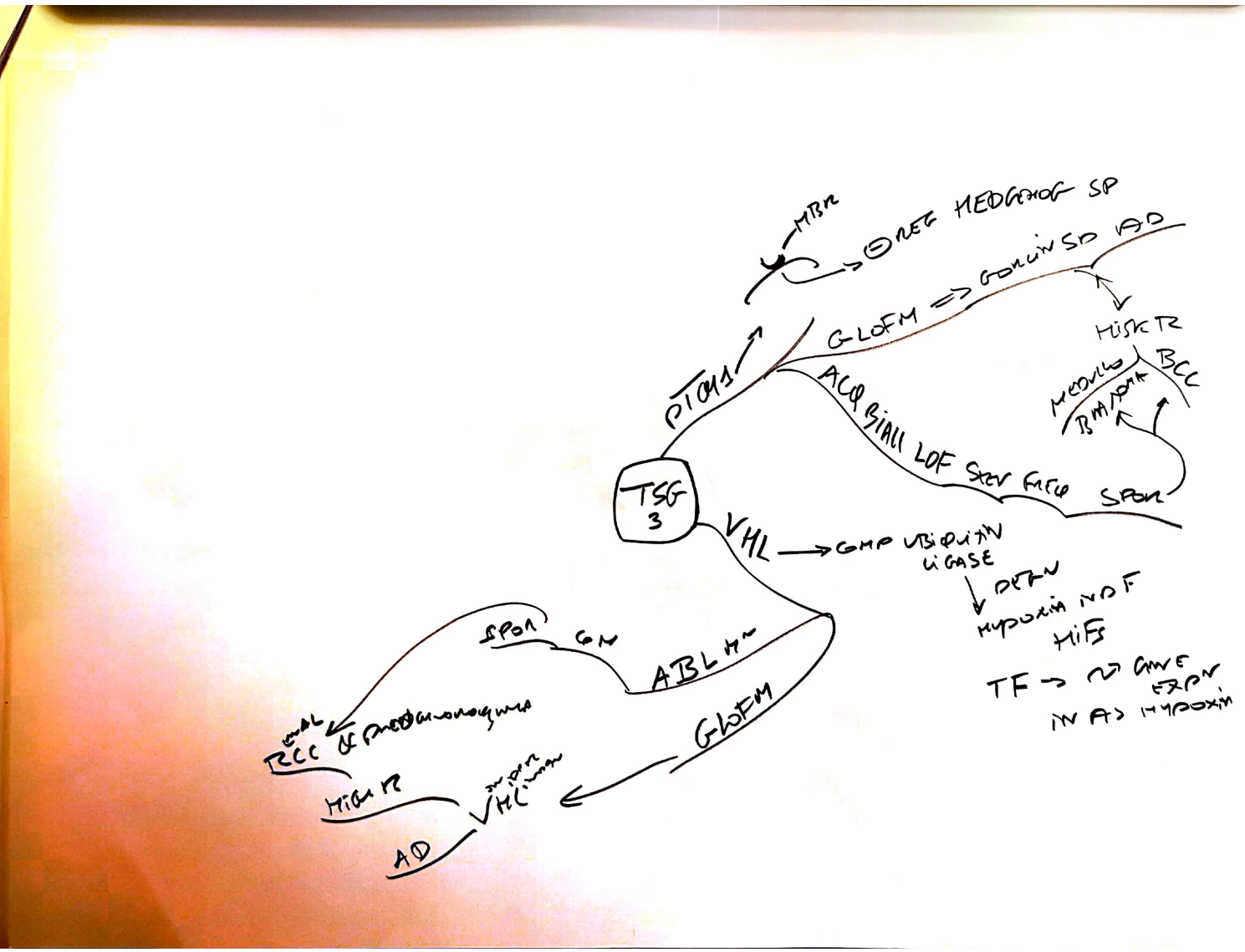
TP53: GUARDIAN GENOME
DNA DAM
DNA DAM & HYPOXIA
"ONCOGENIC" STRESS
ATM / ATR
ATM.ATR
ARREST AT G1/S
CDK i P21
ACTIVITY
APOP
ARREST
DNA DAM
INAPPROPRIATE SIGNALLING BY MUTED ONC P
ANOXIA
TRANSIENT
P53-IND SENESCENCE
P53-IND APOP
P53
RAS
SINGLE MOST COMMON DOM ONC
1/3
>50%
DNA REP P
G1/S

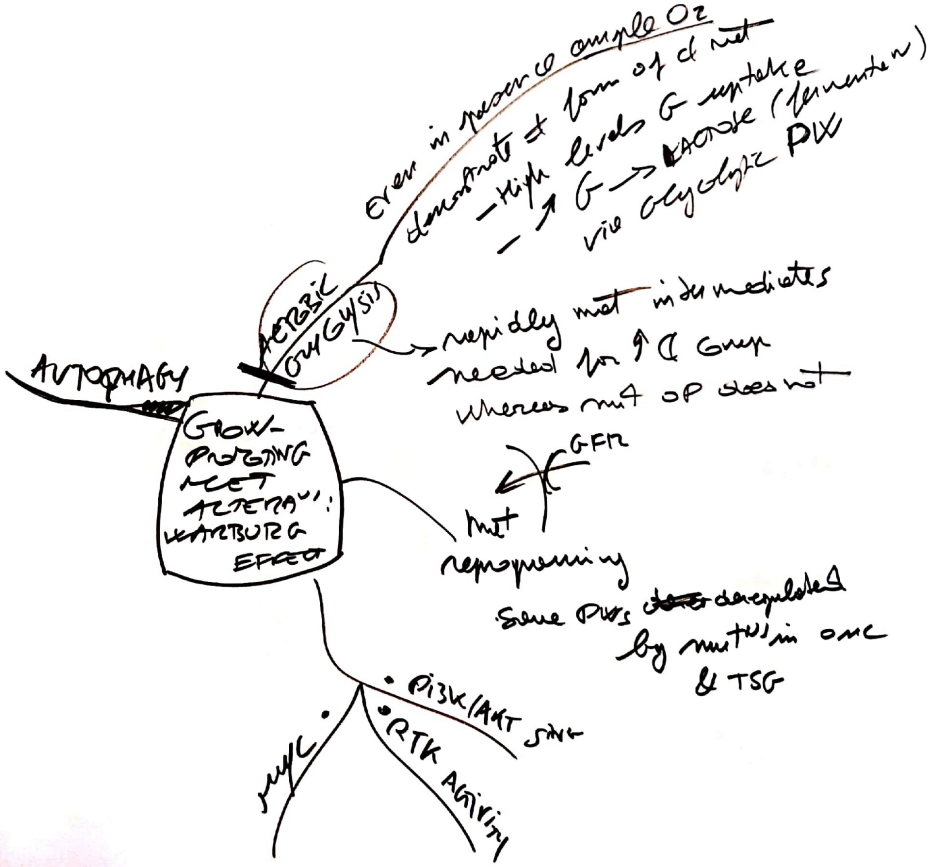

BIALLELIC LOF MUT TP53
RARE LOH
ONE FUNCTIONAL COPY TP53
VERY HIGH INCIDENCE UTERINE VARIETY CANC
=TP53 ↑53
HPV
E6
DNA CANNOT BE REP
TP53
2

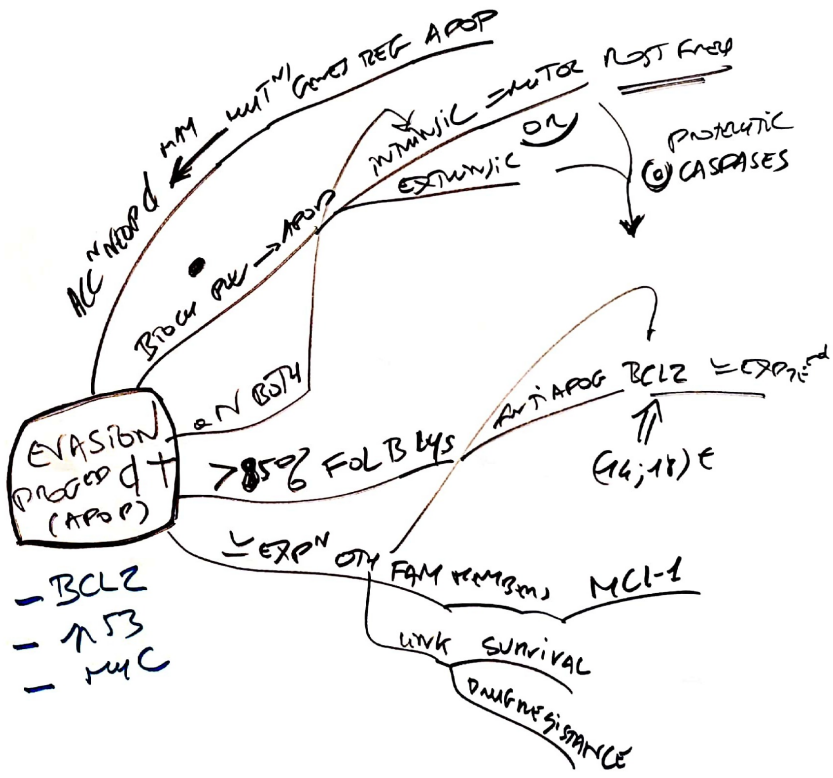


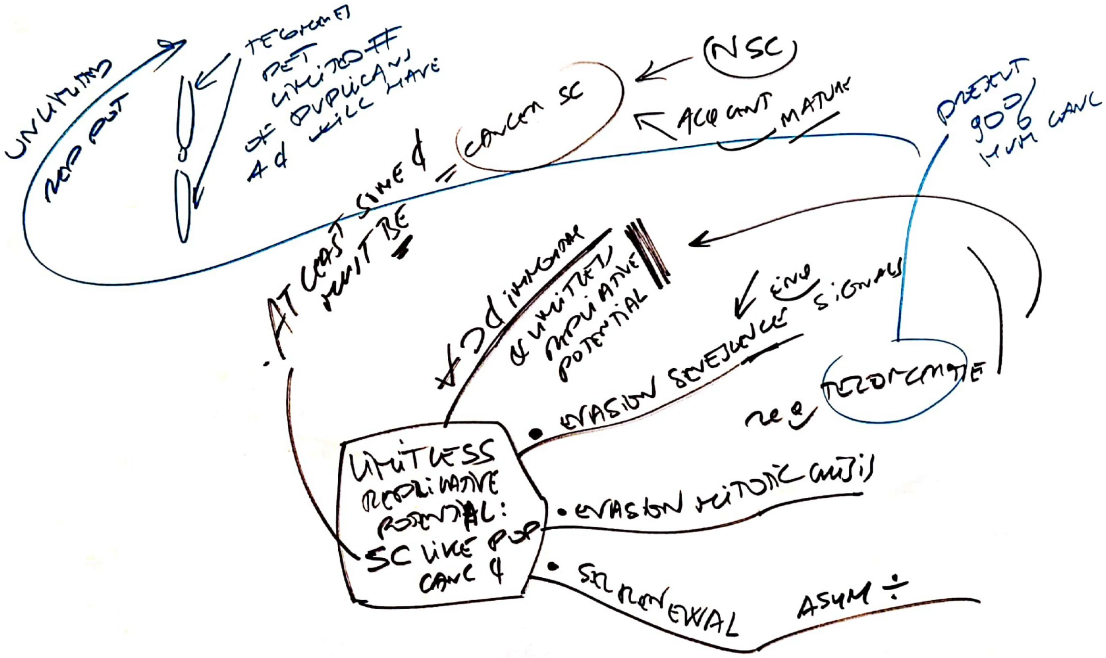
OTHER TUMOR SUPPRESSOR GENES
APC
E-CADHERIN
CDKN2A
TGF-β PATHWAY
COLON
PTEN
NF1
NF2
WT1
WILMS
PATCHED
VHL
LKB1
STK11
FAMILIAL ADENOMATOUS POLYPOSIS
AD
THOUSAND COL POLYPS
COL CA
70% SPOR
ACQUIRED BIALLELIC DEFECTS IN APC
β CATENIN
STOMACH
GERMLINE LOF
CDH1
AD FAM GASTRIC CA
COHESIVENESS
INVASIVENESS
BIALL LOF
MELANOMA
COMPLEX LOCUS
BRCA1 → BREAST
SMADs → G1
RB → EVERYTHING!

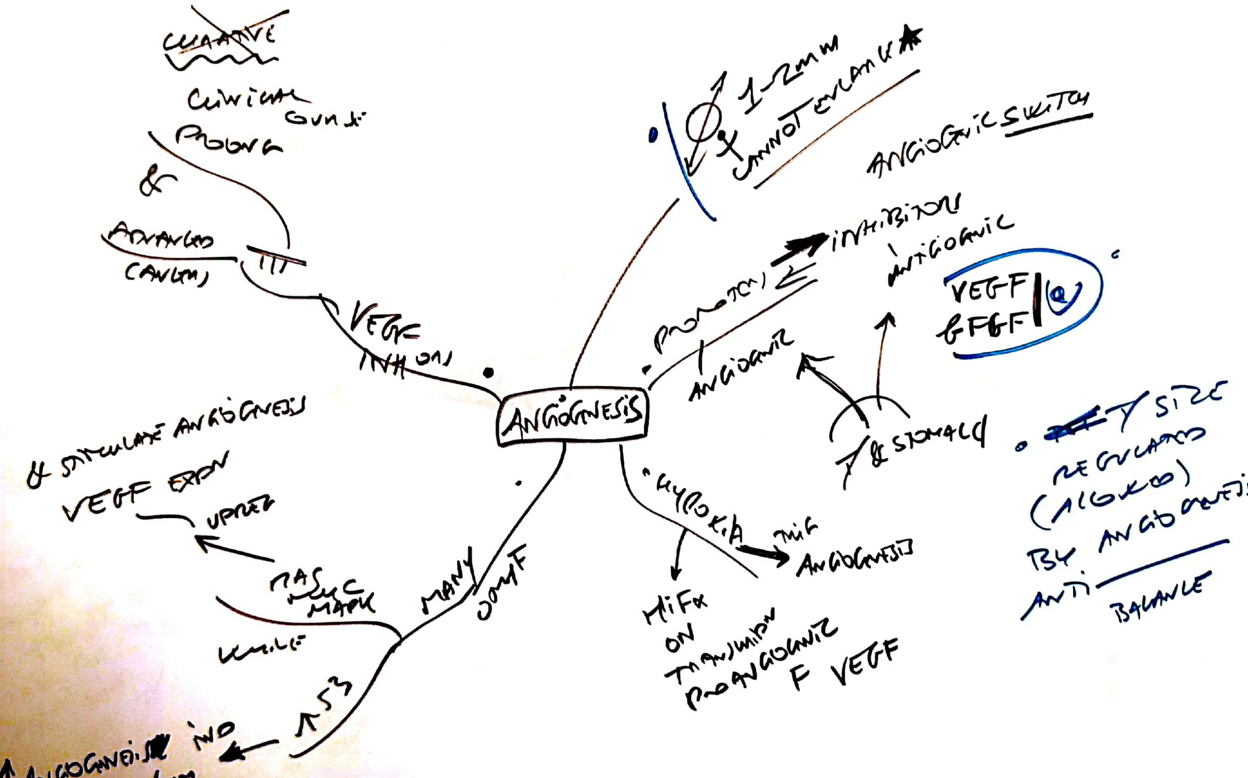

OTH TSG 2
WT1
TF
WILMS T
PED KIDNEY CANC
TGF-B PATH
FREQ LOF TGF BR
SIGNAL TRANSDUCTION
SMADs
PANC
DIV CAs
CARCINOGENESIS
PTEN
PI3K/AKT SIGNALING
BIALL LOF
GERMLINE LOF MUTNS
COWDEN SD
HIGH RISK
AD
NF1
GERMLINE LOF MUTNS
AD
HIGH RISK NF
NEUROFIBROMIN 1
GTPase
REGULATION RAS
NF2
GLOF MUT
HIGH RISK
BILAT SCHWANNOMAS
CONTACT ⊖
CYTOSKEL
MERLIN

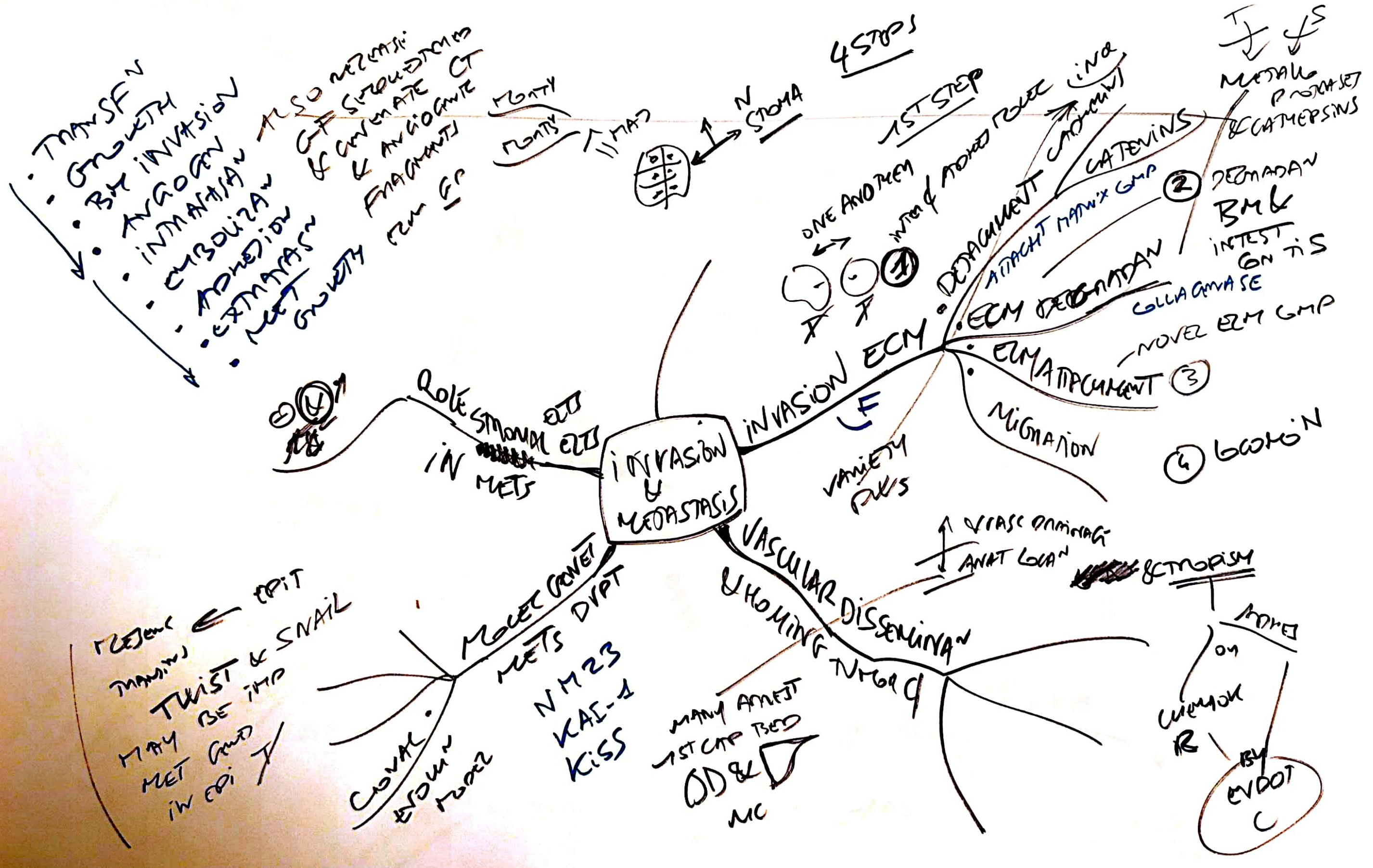

TSG 3
PI3K1
GLOFM
ACQ BIALL LOF
SPON
VHL
SPON
GM
ABL
GLOFM
AD

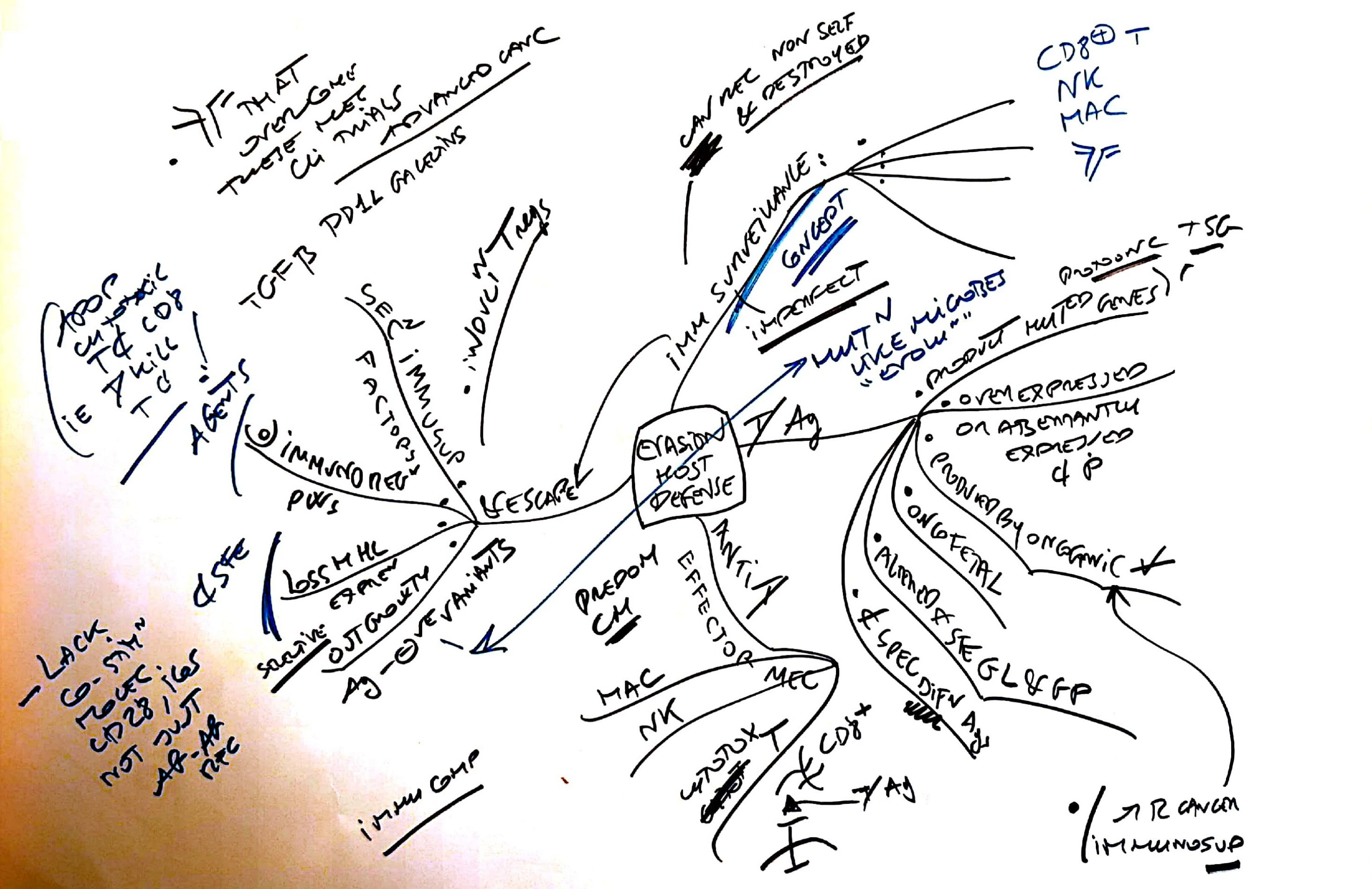

even in presence ample O2
demonstrate a form of d met
- high levels G uptake
- ↑ G → lactate (fermentation)
via acyclic PIK
AEROBIC GLYCOLYSIS
rapidly met intermediates
needed for ↑ G Gmp
whereas mit OP does not
AUTOPHAGY
GROW-PROMOTING MET ALTERATIONS: WARBURG EFFECT
GFR
mit reprogramming
some PIKs deregulated by mut in one & TSG
PI3K/AKT sig
RTK activity
myc


EVASION
PROLIF
(APOP)
- BCL2
- ↑ 53
- MYC
>85% FOLLICULAR
(14;18)
MCL-1
SURVIVAL
DRUG RESISTANCE

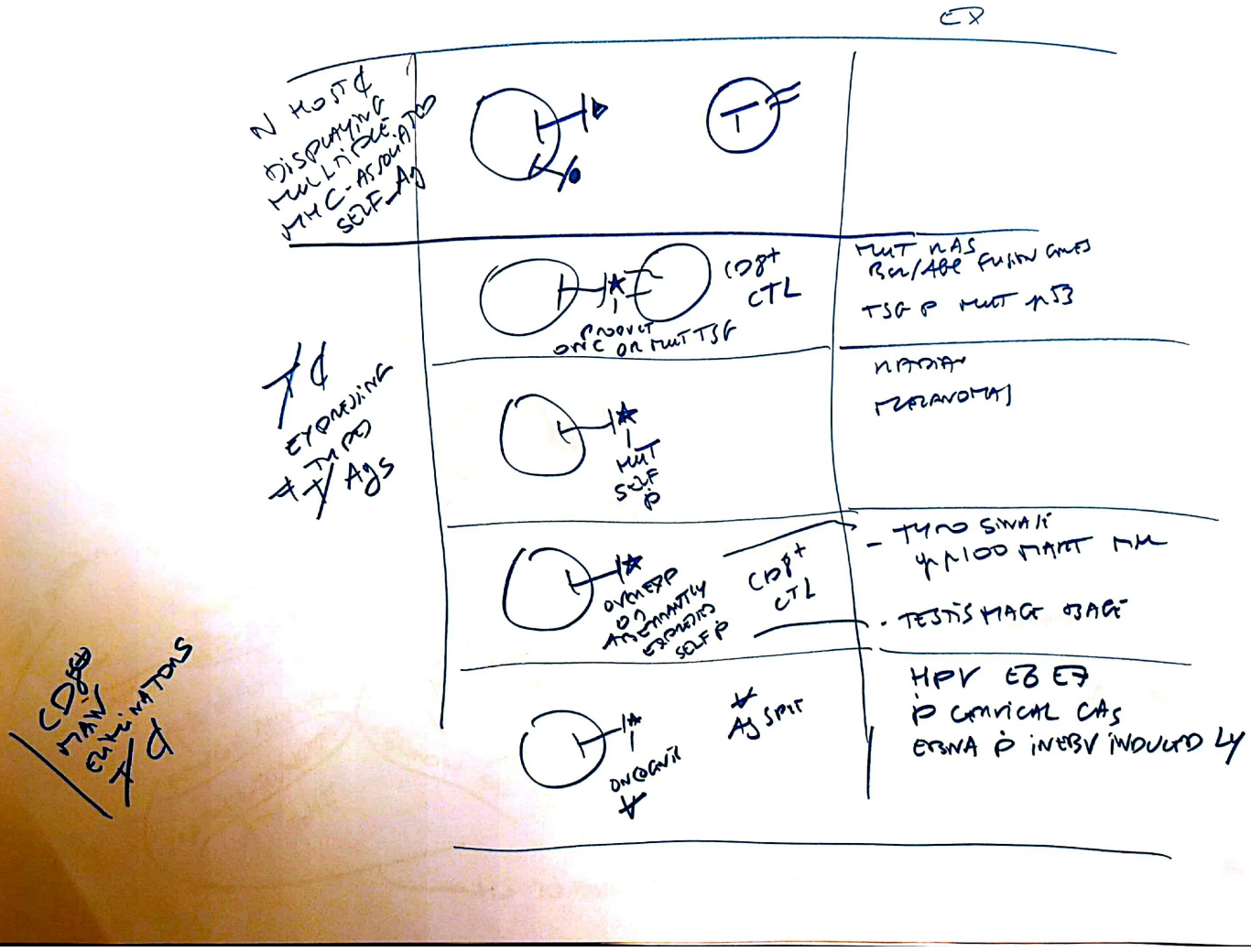

UNLIMITED
REP POT
TELOMERE
PET
LIMITED #
OF DUPLICATN
WILL HAVE
(NSC)
CANCER SC
ACQ CHNT
MATURE
DIRECT
90%
HUM CANC
AT LEAST SOME ¢
PERMIT BE
LIMITLESS
REPLICATIVE
POTENTIAL:
SC LIKE PUP
CANC ¢
EVASION SENESCENCE
EVASION MITOTIC CATS
SELF RENEWAL
ASYM ÷

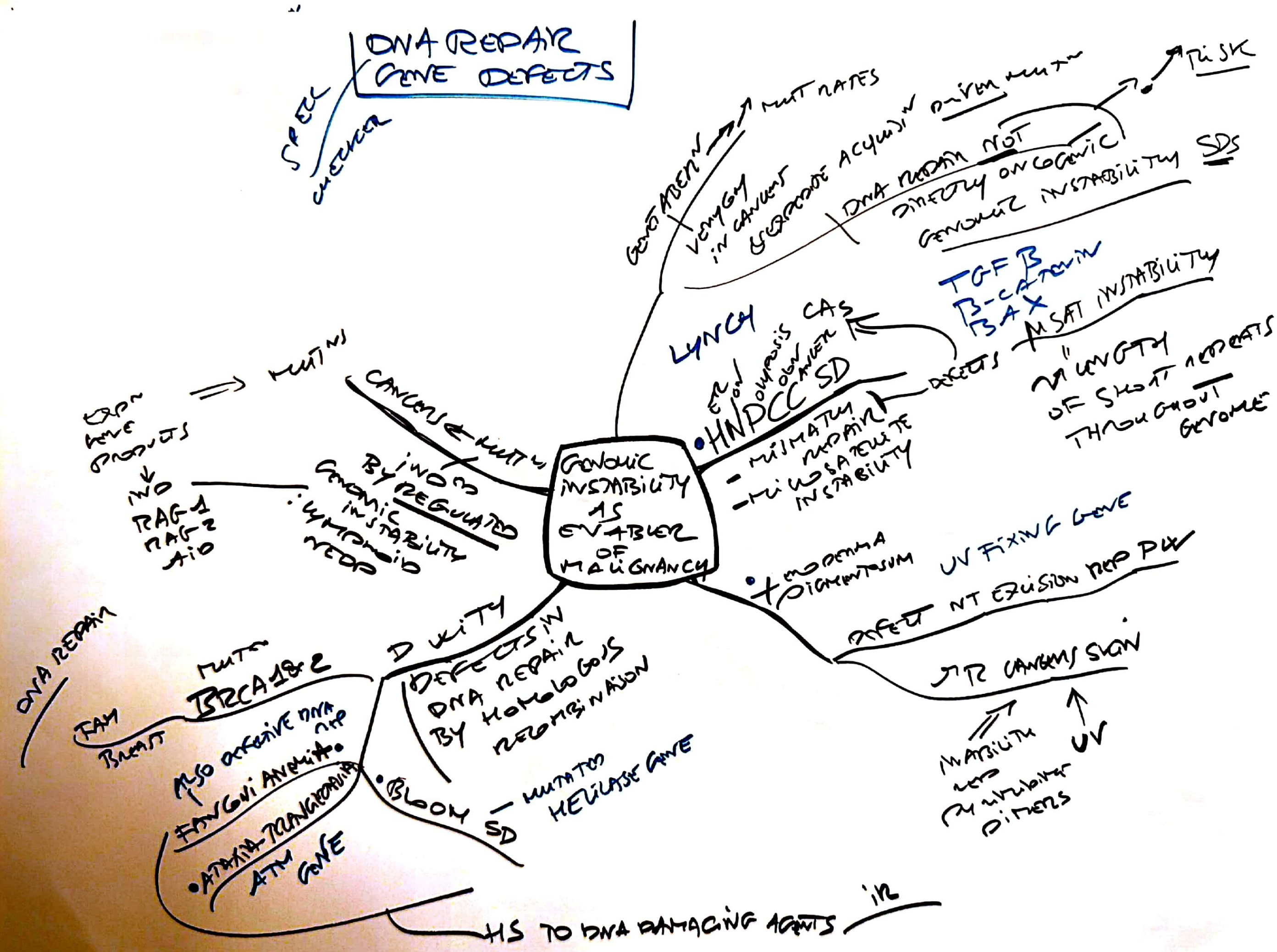

ANGIOGENESIS
VEGF INHIBITORS
ADVANCED CANCERS
CLINICAL
1-2mm
CANNOT ENLARGE
ANGIOGENIC SWITCH
INHIBITORS
ANTIGENIC
PROMOTERS
ANGIOGENIC
VEGF
bFGF
HYPOXIA
ANGIOGENESIS
HIFα
VEGF
SIZE
BY ANGIOGENESIS
ANTI
BALANCE
& STIMULATE ANGIOGENESIS
VEGF EXPN
UPREG
RAS
MAPK
MANY
ONCOF
P53
↑ ANGIOGENESIS IND
INHIB
THROMBOSPONDIN

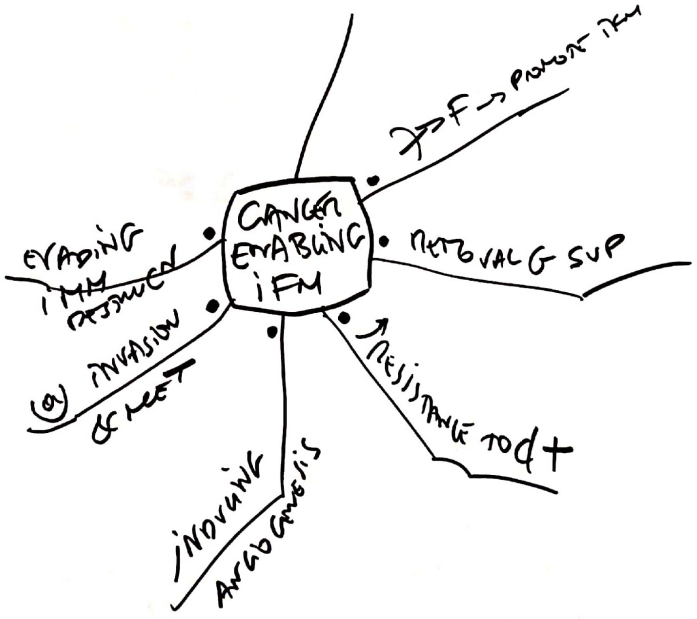

INVASION & METASTASIS
4 STEPS
1ST STEP
INVASION ECM
DETACHMENT
CATENINS
ECM DEGRADATION
COLLAGENASE
ECM ATTACHMENT
MIGRATION
VASCULAR DISSEMINATION & HOMING TUMOR C
MOLEC GENET METS DVPT
NM23
KAI-1
KISS
TWIST & SNAIL
ROLE STROMAL CELLS IN METS
TRANSFN
GROWTH
BM INVASION
ANGIOGEN
INTRAVASAN
EMBOLIZAN
ADHESION
EXTRAVASAN
MET GROWTH

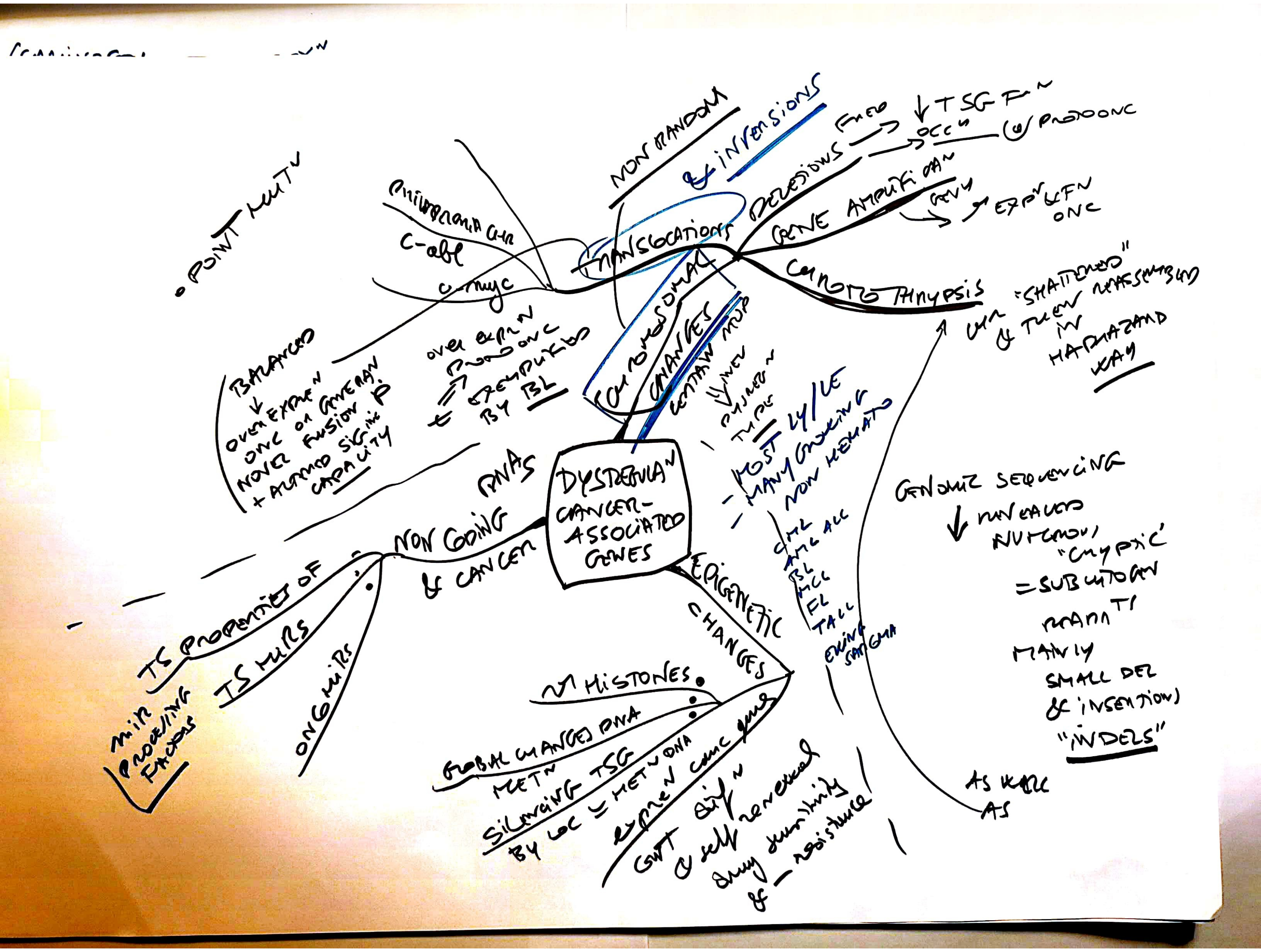


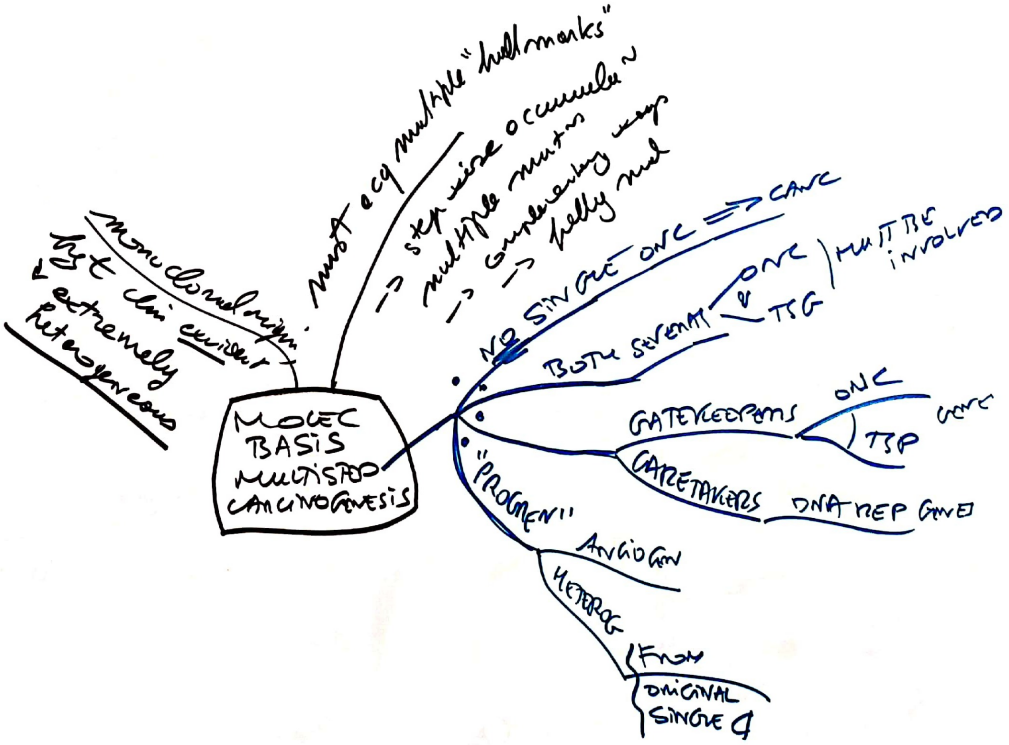
EVASION HOST DEFENSE
IMM SURVEILLANCE:
CD8⊕ T
NK
MAC
CAN REC NON SELF & DESTROYED
ONGOING
IMPERFECT
MUTN LIKE MICROBES "GROW"
T Ag
PRODUCT MUTATED GENES) PROTOONC TSG
OVEREXPRESSED
OR ABERRANTLY EXPRESSED
PRODUCED BY ONCOGENIC V
ONCOFETAL
ALTERED GL & GP
SPEC DIFN Ag
ANTI A
EFFECTOR MEC
PREDOM CM
MAC
NK
CYTOTOX T
CD8+
IMM COMP
ESCAPE
SEC IMMUNOSUP FACTORS
INDUCE Tregs
TGFβ PD1L GALECTINS
IMMUNOREG PWS
AGENTS
LOSS MHC EXPRN
SELECTIVE OUTGROWTH
Ag-ve VARIANTS
LACK CO-STIMN MOLEC CD28, ICOS NOT JUST Ag-Ag REC
THAT OVERCOME THESE MEET CLI TRIALS ADVANCED CANC
R CANCER IMMUNOSUP

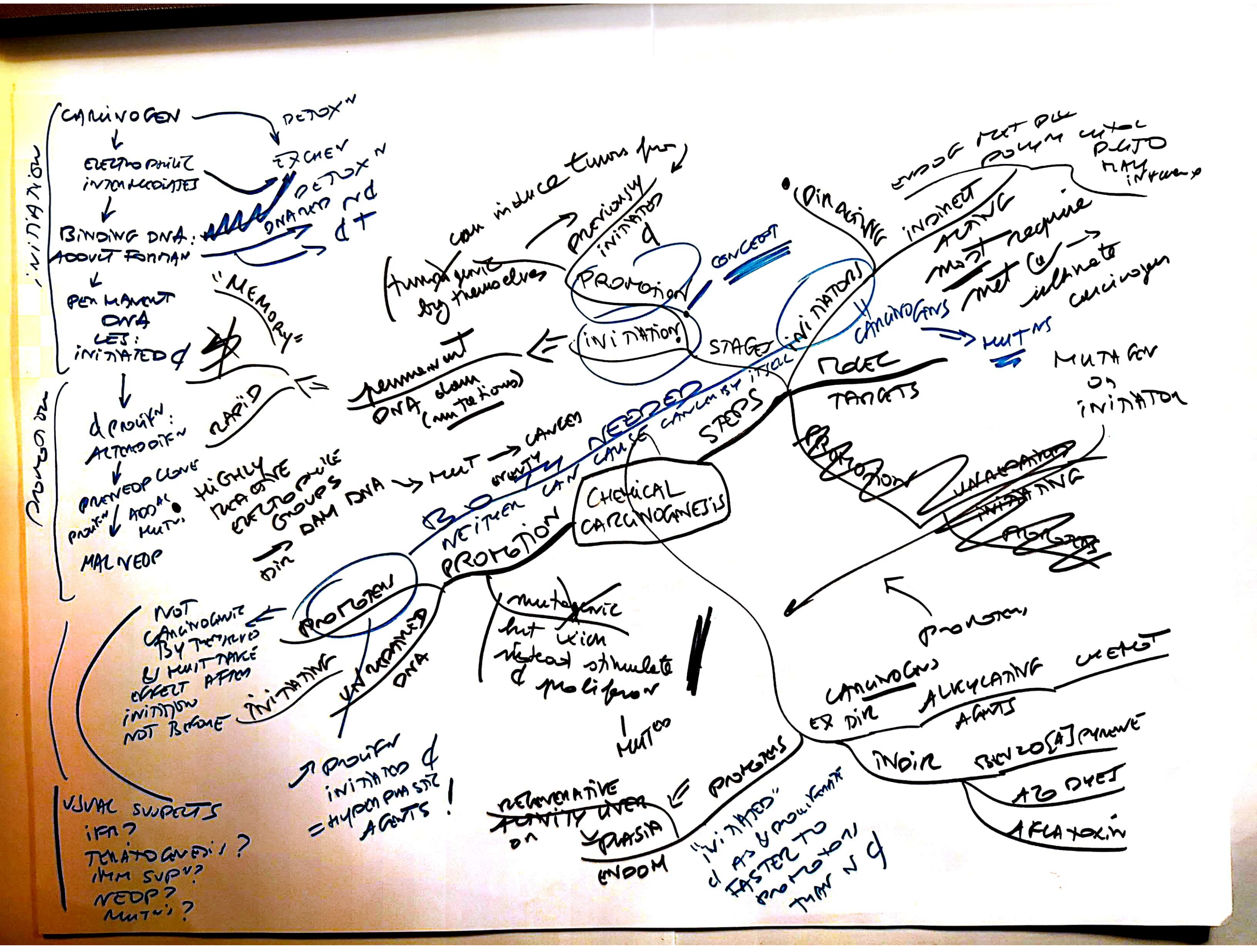


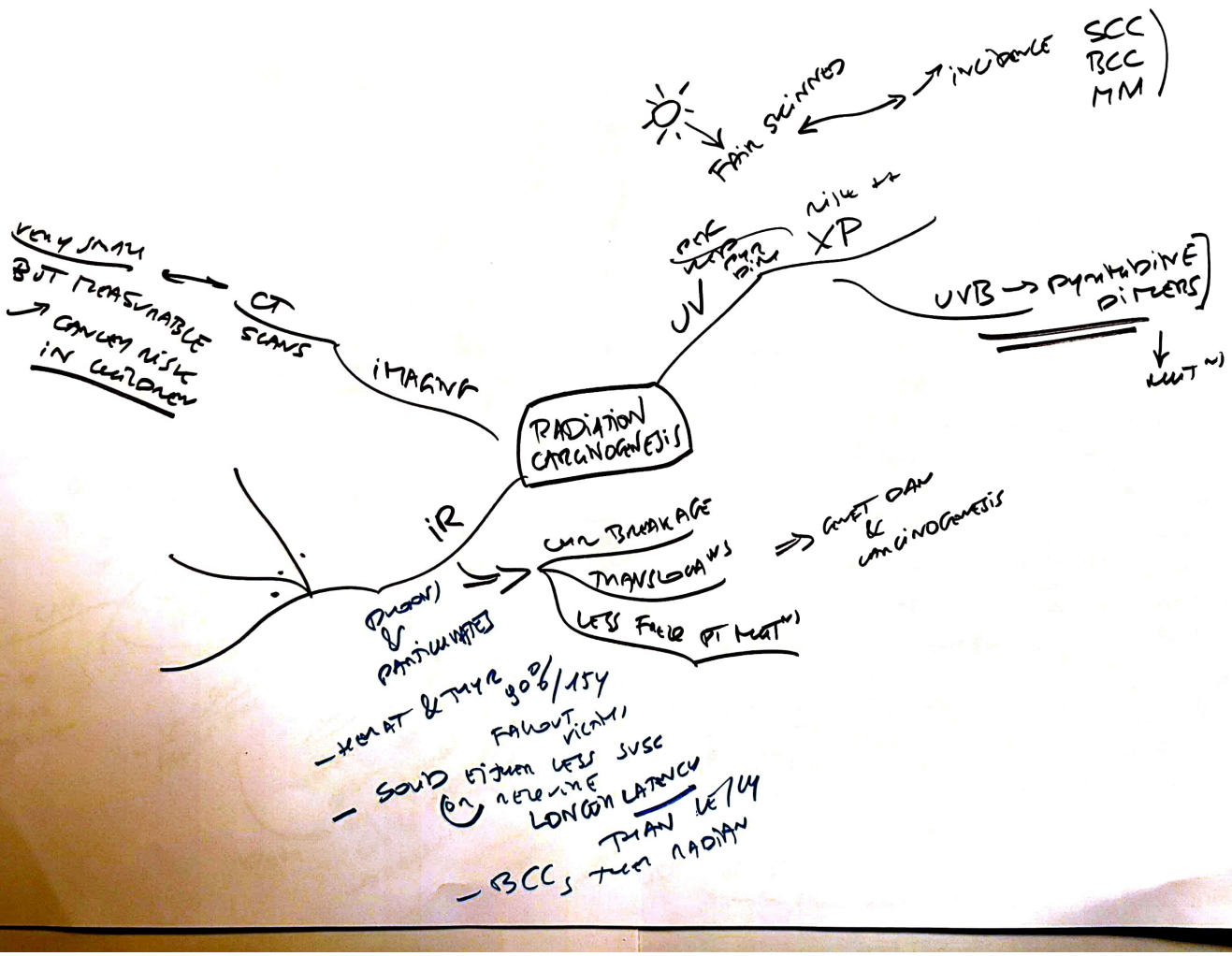

DNA REPAIR GENE DEFECTS
SPELL CHECKER
GENOMIC INSTABILITY AS ENABLER OF MALIGNANCY
MUT RATES
RISK
GENOMIC INSTABILITY
SDs
LYNCH
HNPCC SD
MISMATCH REPAIR
MICROSATELLITE INSTABILITY
DEFECTS
MSAT INSTABILITY
TGF B
B-CATENIN
BAX
OF SHORT REPEATS THROUGHOUT GENOME
XERODERMA PIGMENTOSUM
UV FIXING GENE
DEFECT NT EXCISION REP PW
INABILITY
UV
DIMERS
CANCERS & MUTNS
MUTNS
RAG 1
RAG 2
AID
BY REGULATED GENOMIC INSTABILITY
LYMPHOID NEOP
DEFECTS IN DNA REPAIR BY HOMOLOGOUS RECOMBINATION
DNA REPAIR
BRCA1&2
FAM
BREAST
ALSO DEFECTIVE DNA REP
FANCONI ANEMIA
ATAXIA-TELANGIECTASIA
ATM GENE
BLOOM SD
MUTATED HELICASE GENE
HS TO DNA DAMAGING AGENTS
IR

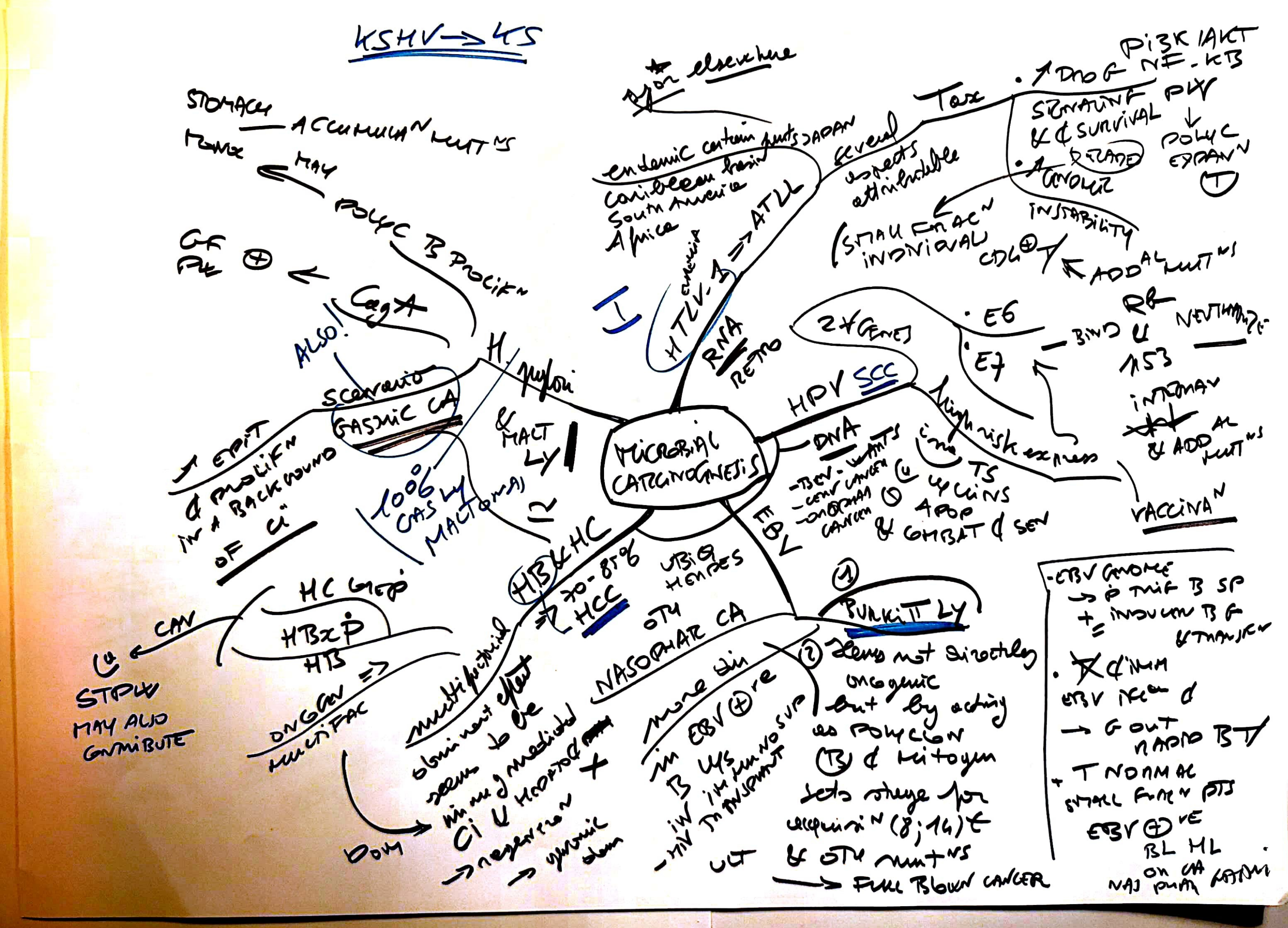

CANCER
ENABLING
iFM


DYSREGULAN CANCER-ASSOCIATED GENES
CHROMOSOMAL CHANGES
TRANSLOCATIONS
& INVERSIONS
NON RANDOM
DELETIONS
↓ TSG FN
GENE AMPLIFICATION
EXPN ONC
CHROMOTHRYPSIS
CHR "SHATTERED" & THEN REASSEMBLED IN HAPHAZARD WAY
c-abl
c-myc
• POINT MUTN
BALANCED
OVER EXPRN ONC OR GENERAN NOVEL FUSION P + ALTERED SIGNG CAPACITY
OVER EXPRN PROTO ONC EXEMPLIFIED BY BL
MOST LY/LE
MANY GROWING NON HEMATO
CML
AML ALL
BL
MCL
FL
TALL
EWING SARCOMA
GENOMIC SEQUENCING
↓ REVEALED NUMEROUS "CRYPTIC" = SUBMICROSC
MANY SMALL DEL & INSERTIONS
"INDELS"
NON CODING RNAS & CANCER
TS PROPERTIES OF
TS MIRS
ONCOMIRS
MIR PROCESSING FACTORS
EPIGENETIC CHANGES
HISTONES
GLOBAL CHANGES DNA METN
SILENCING TSG BY LOC ↑ METN DNA
EXPRN CANC GENE
SELF RENEWAL
DRUG SENSITIVITY OF RESISTANCE

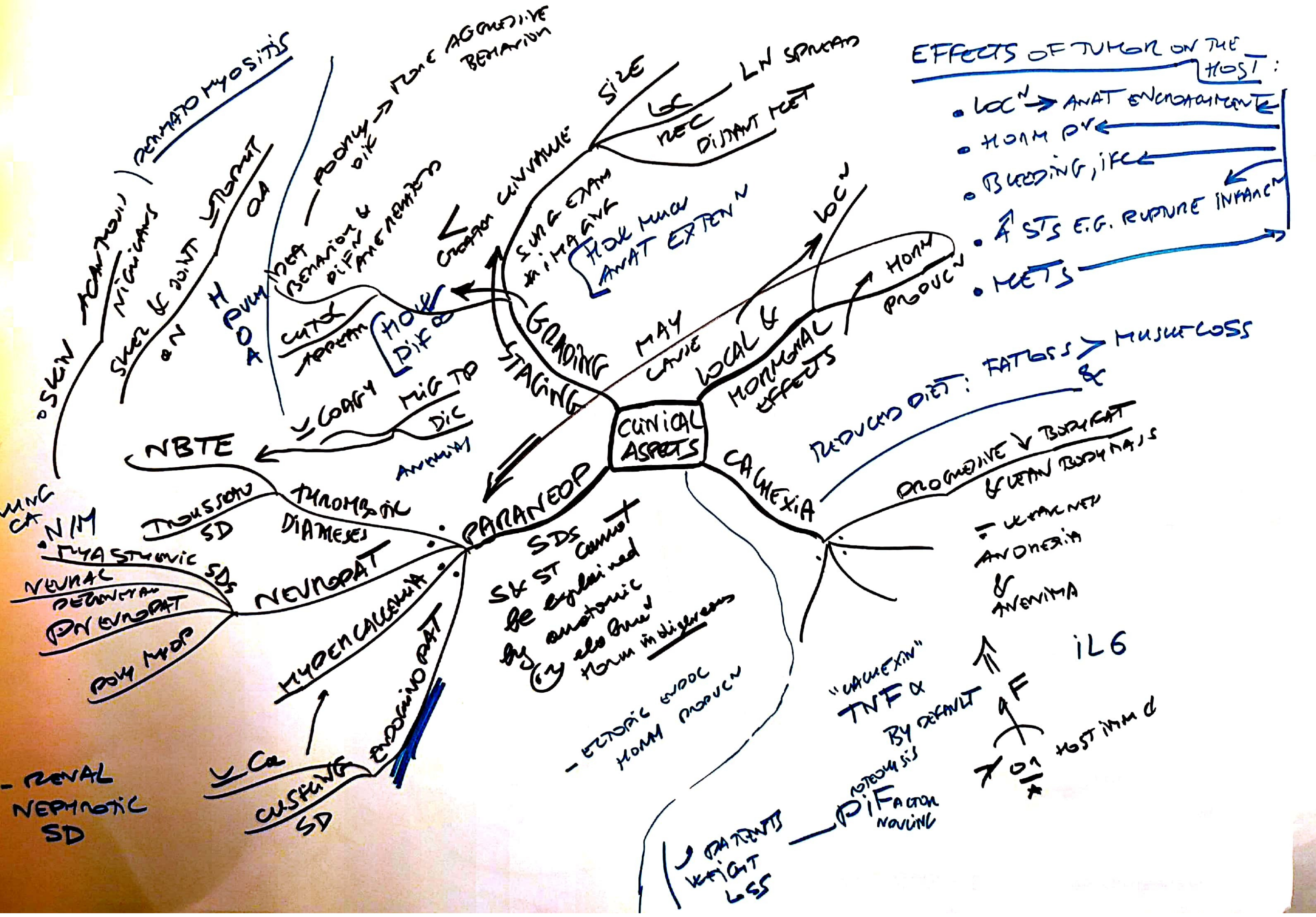

MOLEC BASIS MULTISTEP CARCINOGENESIS
must acq multiple "hallmarks"
-> stepwise accumulation
multiple mutations
-> complementary ways
-> fatally mod
monoclonal origin
but clin evident
extremely heterogeneous
NO SINGLE ONC => CANC
BOTH several ONC & TSG / MULTIPLE involved
GATEKEEPERS ONC TSP
CARETAKERS DNA REP GENES
"PROGRESS" ANGIOGEN
METAPLAS
FROM
ORIGINAL SINGLE


CHEMICAL CARCINOGENESIS
STAGES
STEPS
INITIATION
PROMOTION
CARCINOGEN
DETOX'N
EXCRET
ELECTROPHILIC INTERMEDIATES
BINDING DNA: ADDUCT FORMAN
PERMANENT DNA LES: INITIATED C
"MEMORY"
RAPID
permanent DNA damage (mutations)
C PROLIF'N: ALTERATION
PRENEOP CLONE
ADDAL MUTNS
MALNEOP
HIGHLY REACTIVE ELECTROPHILE GROUPS
DAM DNA → MUT → CANCER
DIR
NEITHER CAN CAUSE CANCER BY ITSELF
BOTH NEEDED
CONCEPT
INITIATORS
PROMOTERS
can induce tumours from previously initiated C
tumorigenic by themselves
NOT CARCINOGENIC BY THEMSELVES
EFFECT AFTER INITIATION NOT BEFORE
INITIATING
UNREPAIRED DNA
mutagenic
but rich
stimulate C proliferation
MUTNS
PROLIF'N INITIATED C
= HYPERPLASTIC AGENTS!
REGENERATIVE ACTIVITY LIVER
HYPERPLASIA
ENDOM
"INITIATED" C AS PROLIFERATE FASTER TO PROMOTION THAN N C
DIR ACTING
INDIRECT ACTING
most require met C
CARCINOGENS = MUTNS
MUTAGEN ON INITIATOR
MOLEC TARGETS
PROMOTION
CARCINOGENS
EX DIR
ALKYLATING AGENTS
INDIR
BENZO[A]PYRENE
AZO DYES
AFLAXOXIN
PROMOTERS
VISUAL SUSPECTS
IFN?
TERATOGENESIS?
IMM SUPN?
NEOP?
MUTNS?

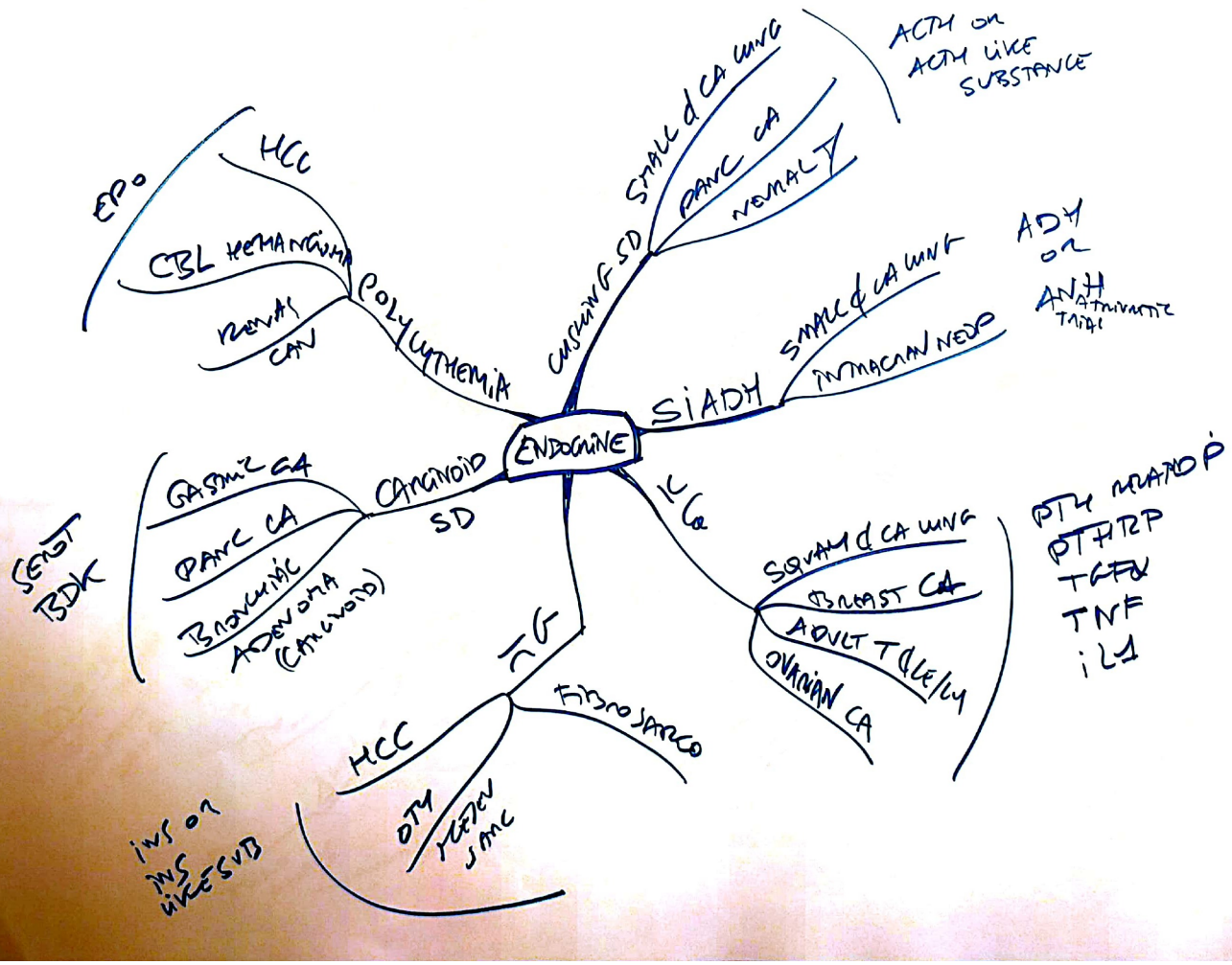

RADIATION CARCINOGENESIS
UV
XP
UVB → PYRIMIDINE DIMERS
SCC
BCC
MM
INCIDENCE
FAIR SKINNED
IMAGING
CT SCANS
VERY SMALL
BUT REASONABLE
CANCER RISK
IN CHILDREN
IR
(RADON)
& PARTICULATES
DNA BREAKAGE
TRANSLOCATIONS
LESS FREE RADICALS
⇒ CAUSE OF
CARCINOGENESIS
FALLOUT
VICTIMS
LONGER LATENCY
THAN UV
BCC's

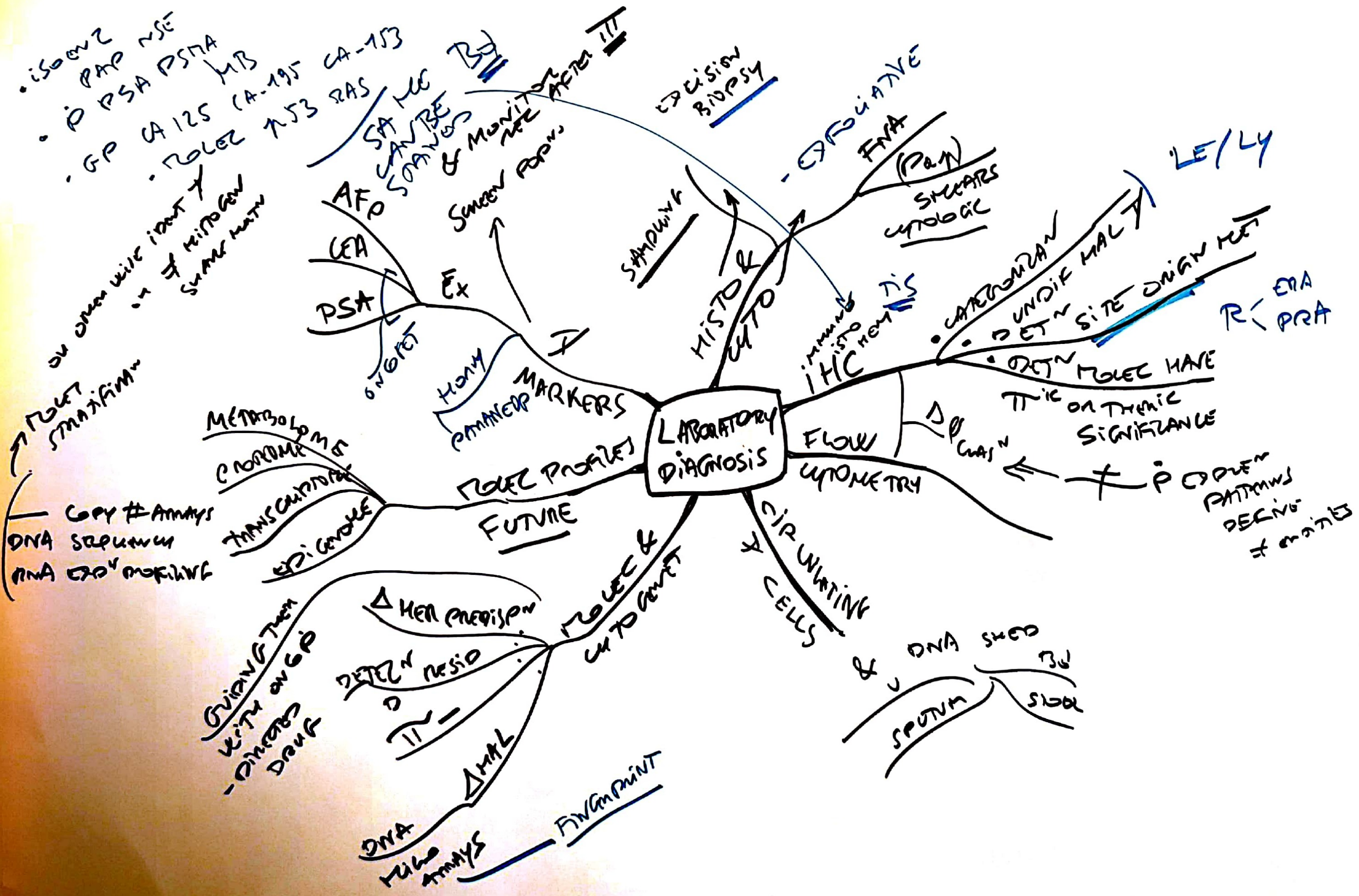


KSHV => KS
MICROBIAL CARCINOGENESIS
H. pylori
GASTRIC CA
CagA
ALSO!
POLYC B PROLIF
GF
STOMACH
ACCUMULATION
MAY
↑ EPIT
& MACT LY
100% CASES LY MACTOMAS
HBV HCV
70-85% HCC
OTH
HBx
HB
HC
UBIQ
multifactorial
NASOPHAR CA
more in EBV ⊕ve
in B LYS
EBV
BURKITT LY
DNA
HPV SCC
high risk express
E6
E7
BIND
RB
153
VACCINATION
RNA
RETRO
HTLV-1 => ATLL
endemic certain parts JAPAN
Caribbean basin
South America
Africa
Tax
several aspects attributable
SMALL FRACTION INDIVIDUAL
↑ PROLIF
SIGNALING
& ¢ SURVIVAL
NF-KB
PI3K/AKT
POLYC EXPANSION
INSTABILITY
ADD MUTNS
seems not directly oncogenic
but by acting as POLYCLON B ¢ mitogen
sets stage for acquisition (8;14) t
& OTH MUTNS
→ FULL BLOWN CANCER



EFFECTS OF TUMOR ON THE HOST:
• LOCN → ANAT ENCROACHMENT
• HORM PR
• BLEEDING, IFC
• ↑ STs E.G. RUPTURE INFARCN
• METS
CLINICAL ASPECTS
GRADING
STAGING
SIZE
LN SPREAD
LOC
REG
DISTANT MET
SURG EXAM & IMAGING
HOW MUCH ANAT EXTENN
HOW DIF
LOCAL & HORMONAL EFFECTS
LOCN
HORM PRODUCN
MAY CAUSE
CACHEXIA
REDUCED DIET: FAT LOSS > MUSCLE LOSS
PROGRESSIVE ↓ BODY FAT & LEAN BODY MASS
WEAKNESS
ANOREXIA
& ANEMIA
IL6
"CACHEXIN" TNF α
BY DEFAULT
PIF FACTOR
PATIENTS WEIGHT LOSS
PARANEOP
SDs
S & ST cannot be explained by anatomic (or) elaborated horm indigenous
ECTOPIC ENDOC HORM PRODUCN
THROMBOTIC DIATHESES
TROUSSEAU SD
NBTE
MIG TO DIC
ANEMIA
NEUROPAT
MYASTHENIC SDs
NEURAL DEGENERATION
PERIPH NEUROPAT
POLYMYOP
HYPERCALCEMIA
ENDOCRINOPAT
CUSHING SD
RENAL
NEPHROTIC SD
SKIN ACANTHOSIS NIGRICANS
DERMATOMYOSITIS
SKEL & JOINT
OA
H O A


ENDOCRINE
POLYCYTHEMIA
EPO
HCC
CBL HEMANGIOMA
RENAL CAN
CUSHING'S SD
SMALL d CA LUNG
PANC CA
NORMALY
ACTH OR ACTH LIKE SUBSTANCE
SiADH
SMALL d CA LUNG
INTRACRAN NEOP
ADH OR AVP ARGININE VASOPRESSIN
CARCINOID SD
GASTRIC CA
PANC CA
BRONCHIAL ADENOMA (CARCINOID)
SENT BDK
IL6
SQUAM d CA LUNG
BREAST CA
ADULT T CELL/LY
OVARIAN CA
PTH HEAD PTHRP TGFa TNF IL1
IL6
FIBROSARCO
HCC
OTH
KIDNEY CANC
INFO ON INCREASED


LABORATORY DIAGNOSIS
MARKERS
HISTO & CYTO
IHC
FLOW CYTOMETRY
CIRCULATING CELLS
MOLEC & CYTOGENET
MOLEC PROFILES
FUTURE
SAMPLING
EXCISION BIOPSY
EXFOLIATIVE
FNA
SMEARS
CYTOLOGIC
AFP
CEA
PSA
ONCOFET
METABOLOME
PROTEOME
TRANSCRIPTOME
EPIGENOME
COPY # ARRAYS
DNA SEQUENCING
SITE ORIGIN MET
MOLEC MARK
SPUTUM
DNA SHED
STOOL
DNA
MICRO ARRAYS
FINGERPRINT
ER
PRA