

Muligheter og utfordringer ved diagnostikk av lungekreft

Marius Lund-Iversen

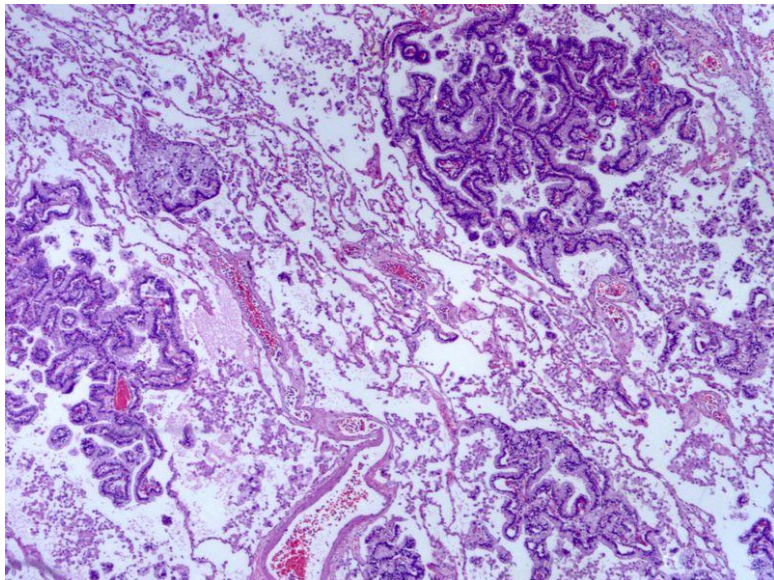
Avd. for patologi Oslo universitetssykehus

Interessekonflikter

- Foredrag for Lilly
- Møte i regi av Roche
- Kurs i regi av MSD om tolkning av PD-L1

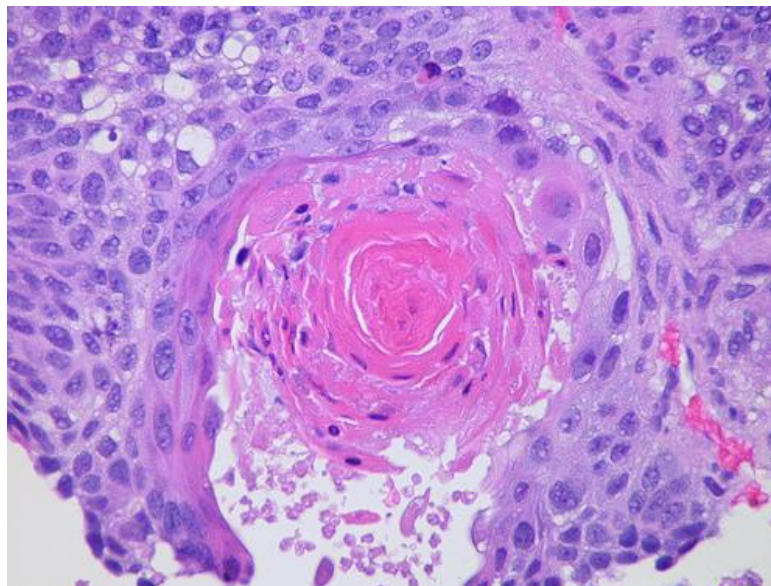
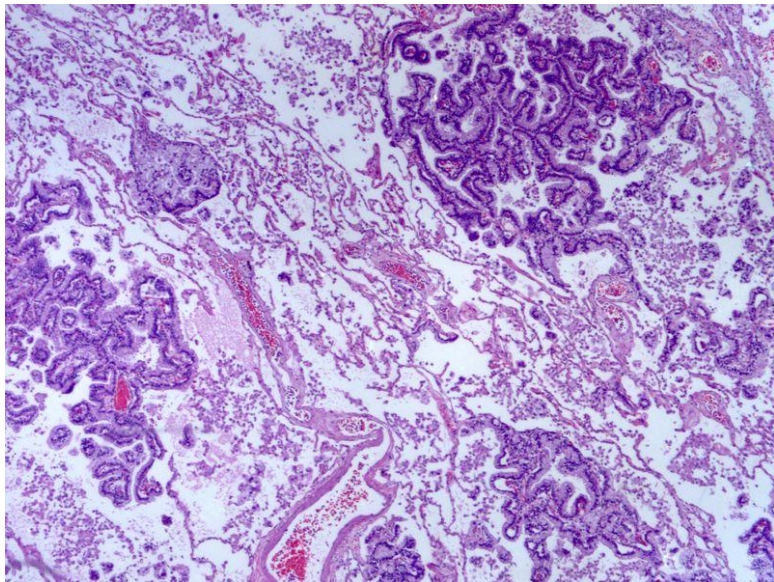
Muligheter

- Histologisk klassifikasjon
 - Adenokarsinom



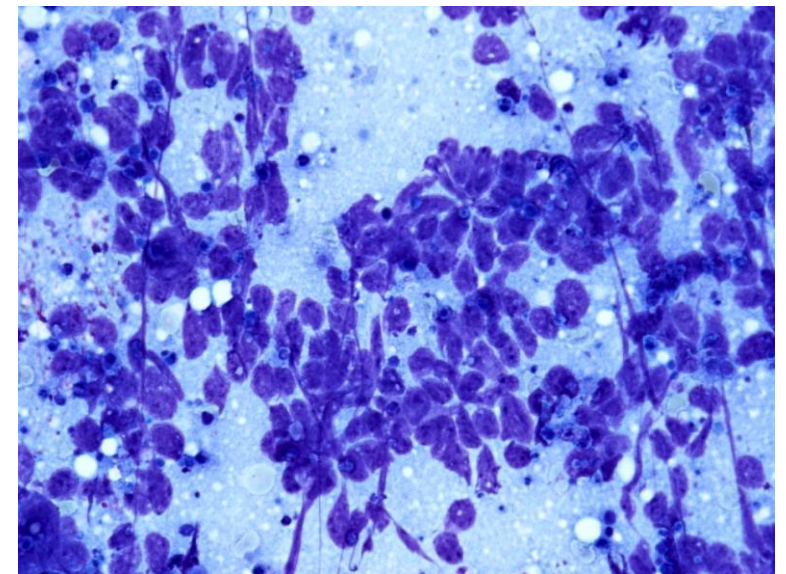
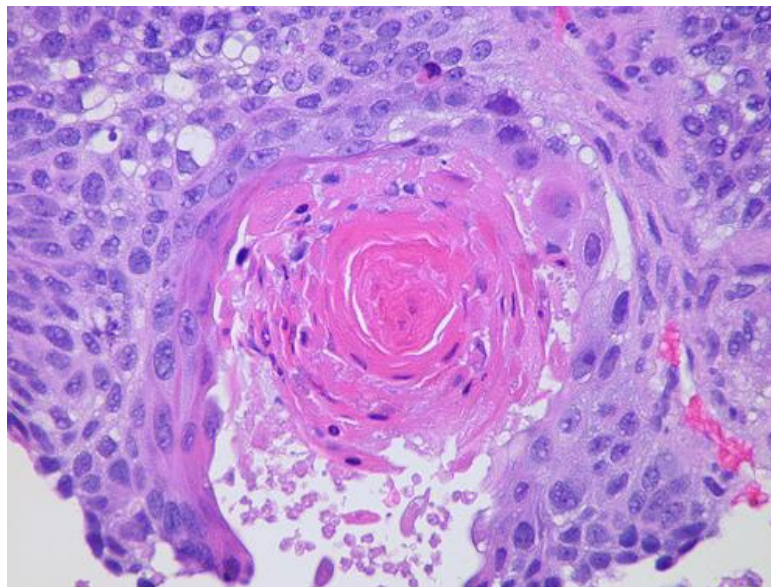
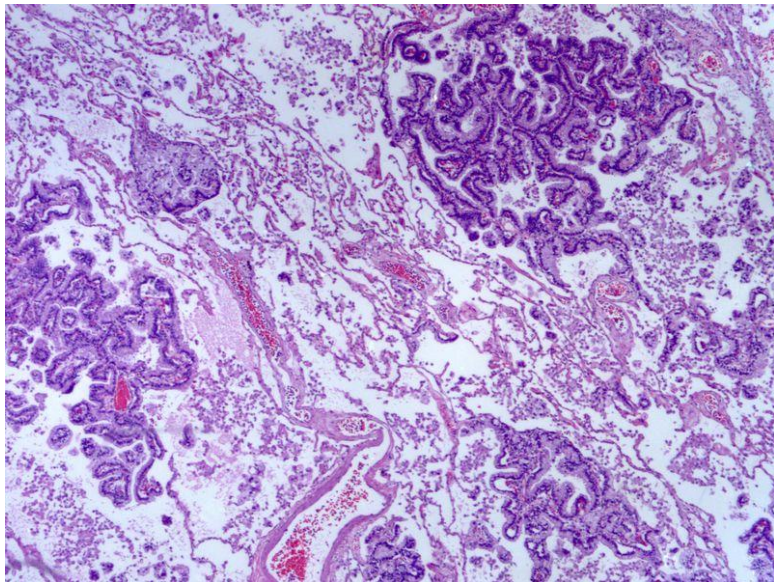
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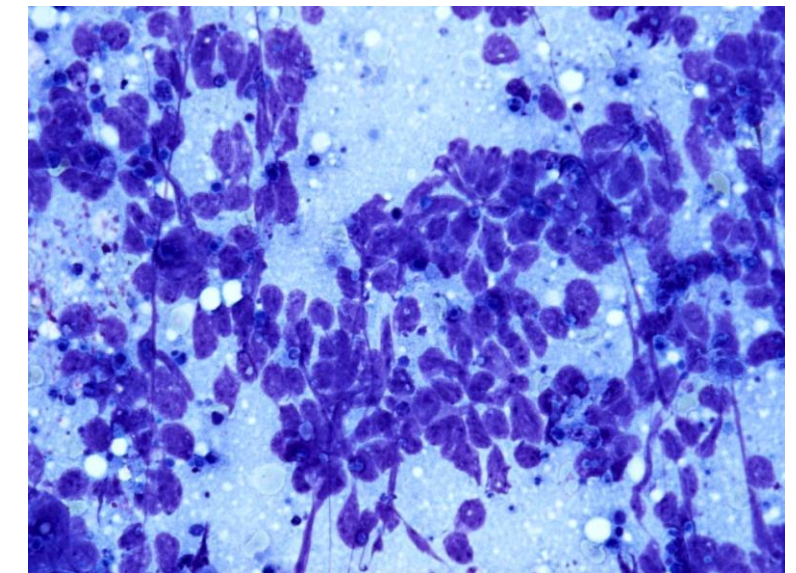
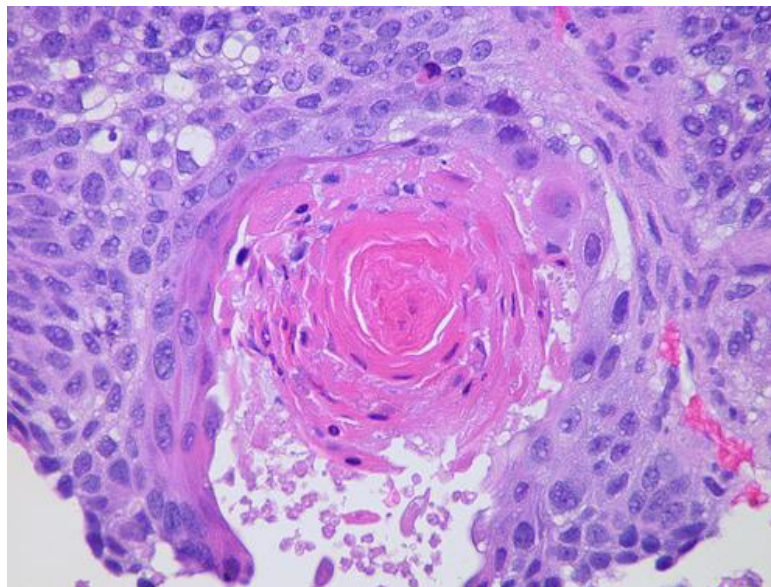
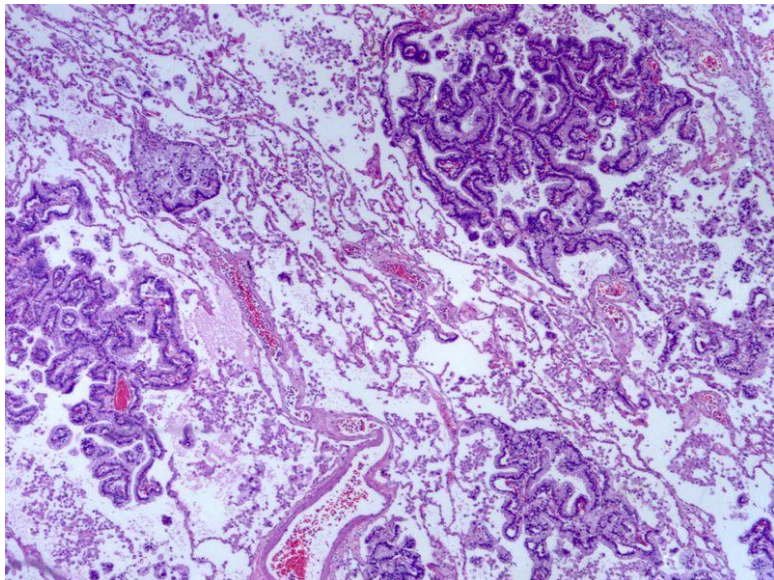
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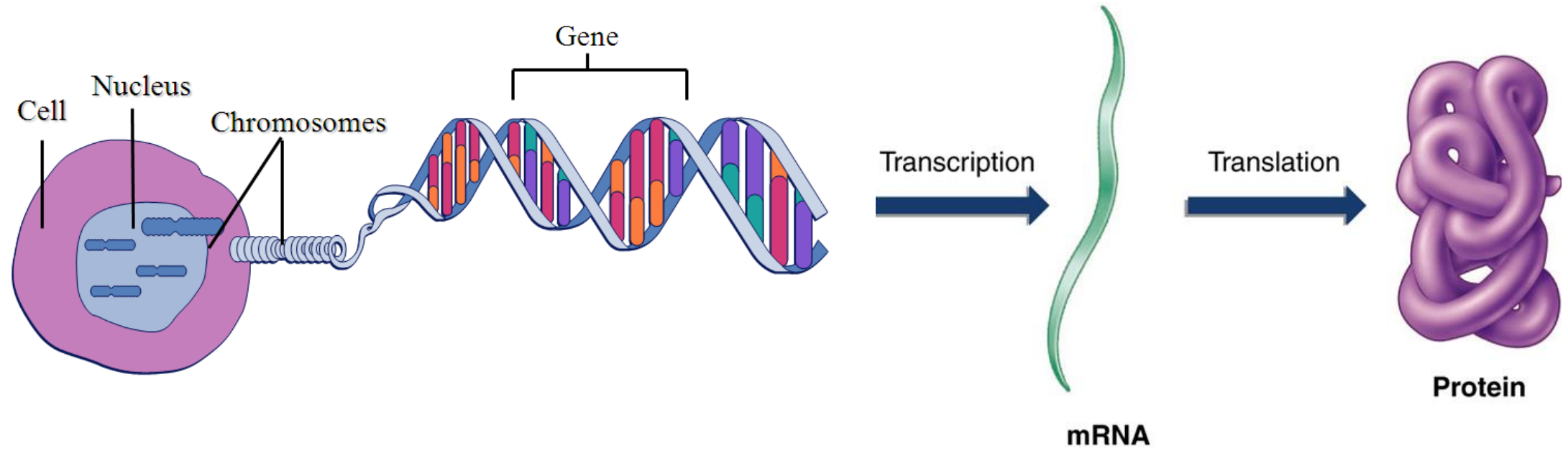
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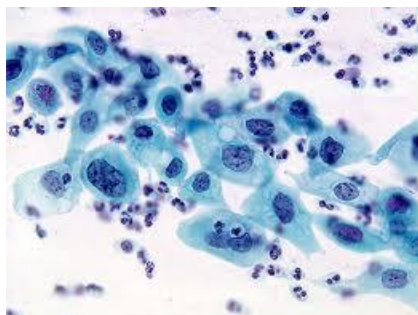
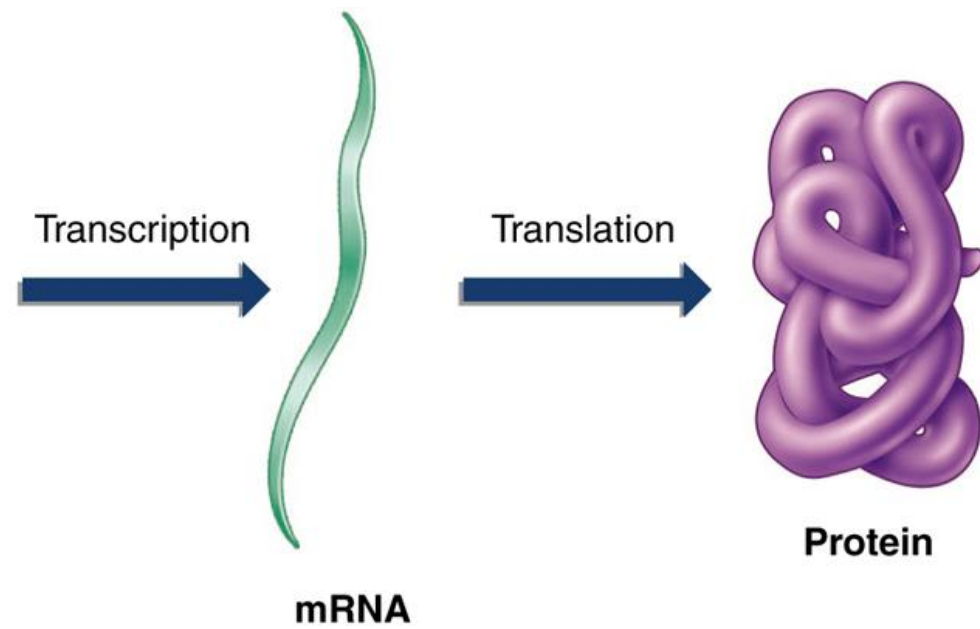
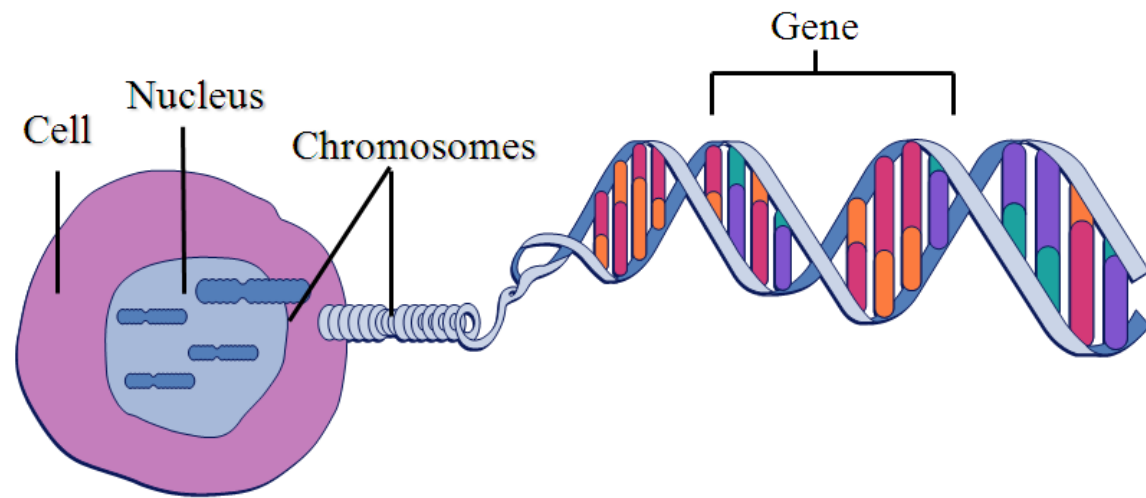
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 - Småcellet karsinom
 - Annen type tilstand og/eller svulst

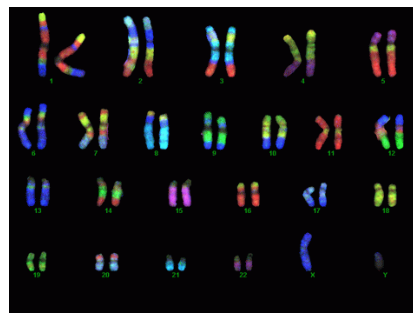
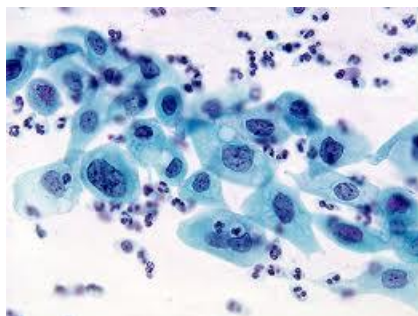
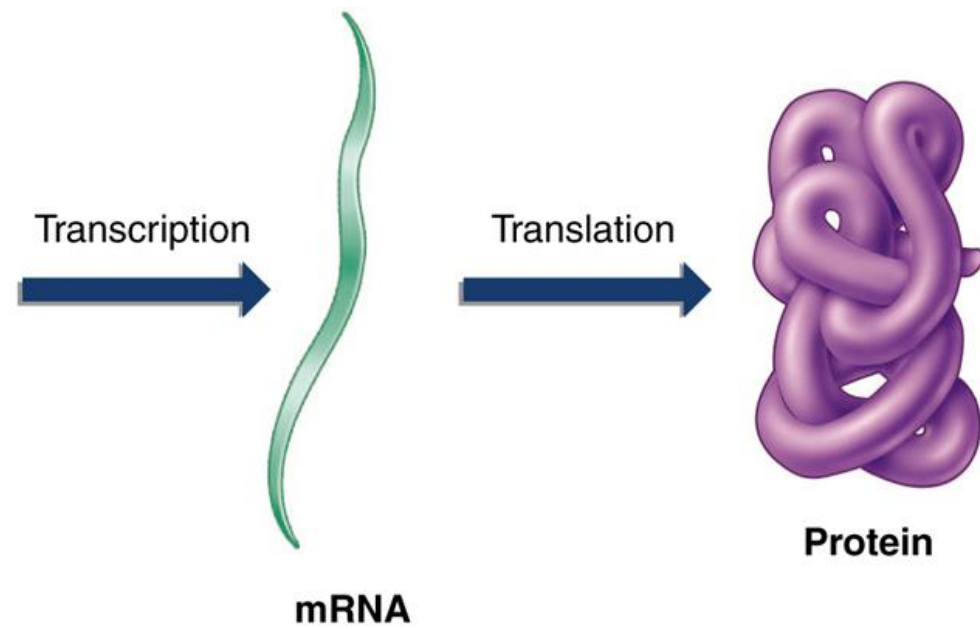
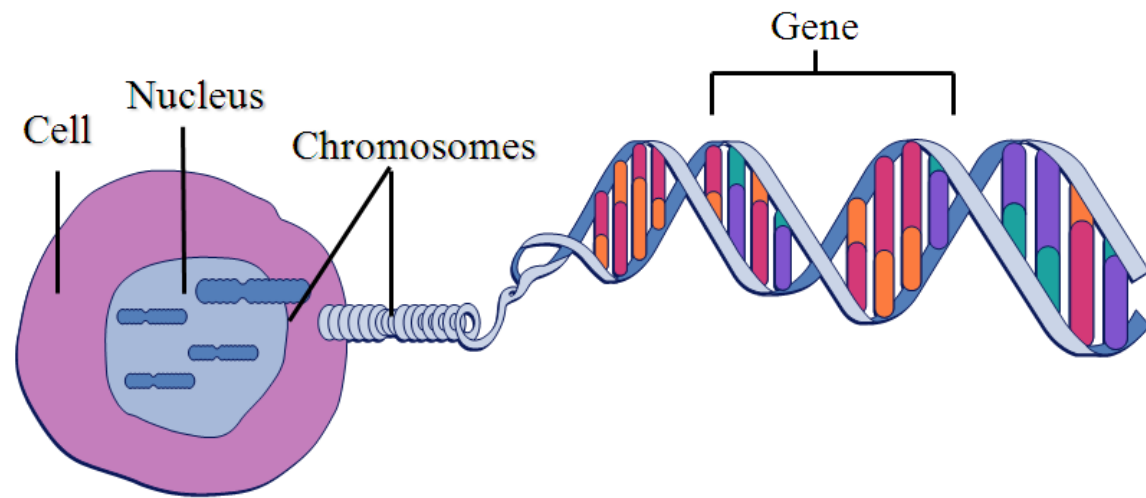


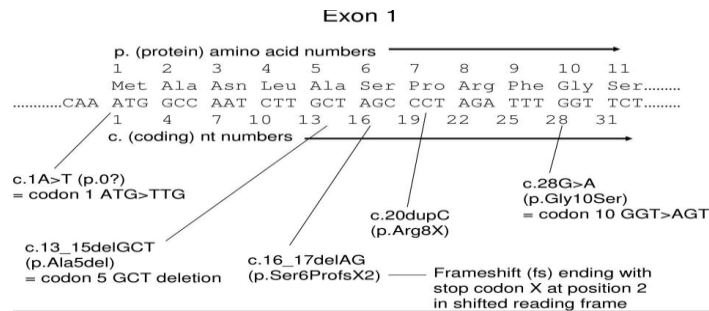
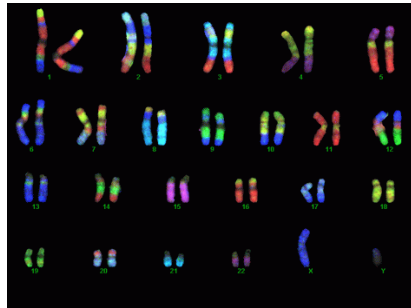
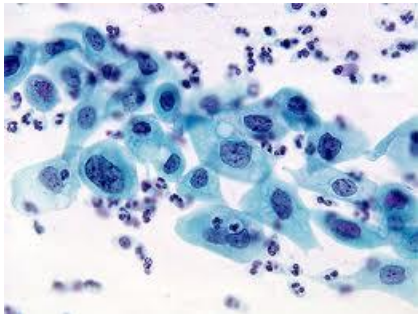
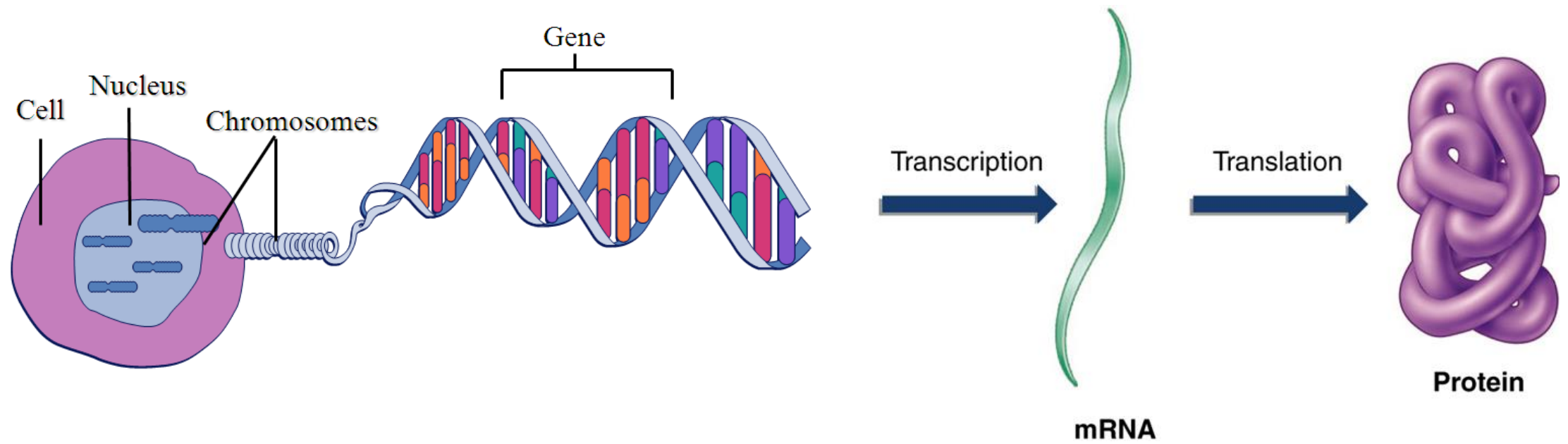
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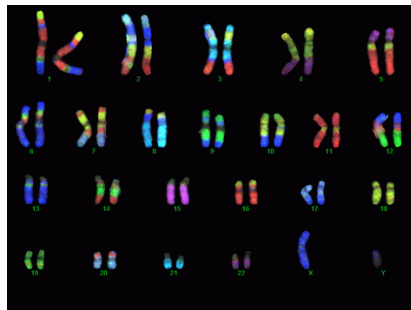
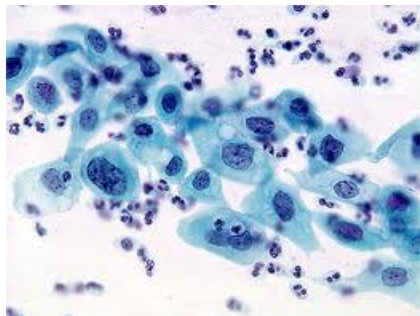
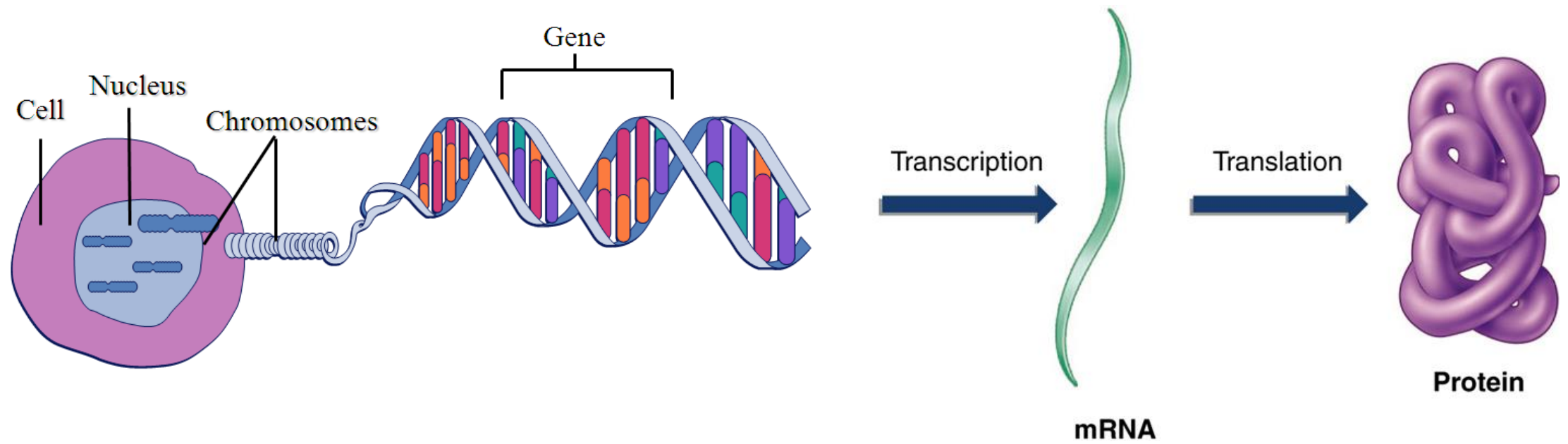
- Genetisk klassifikasjon
 - Forskjellige avvik i arveanlegget
 - RNA vs DNA + + + + +
 - Proteiner
- **ctDNA (blod)**







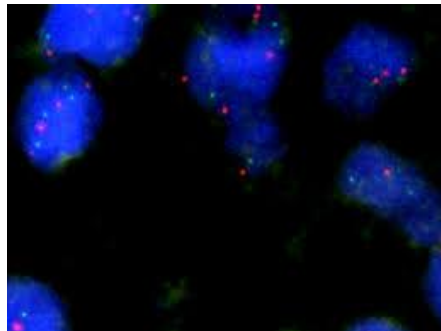


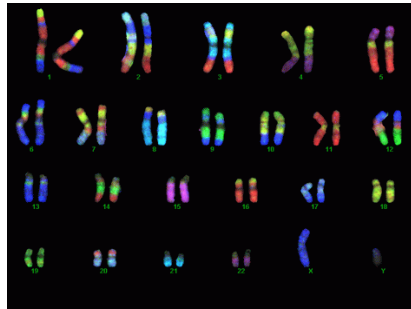
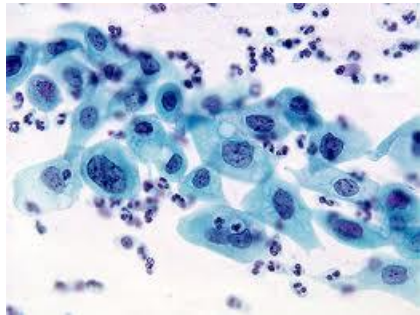
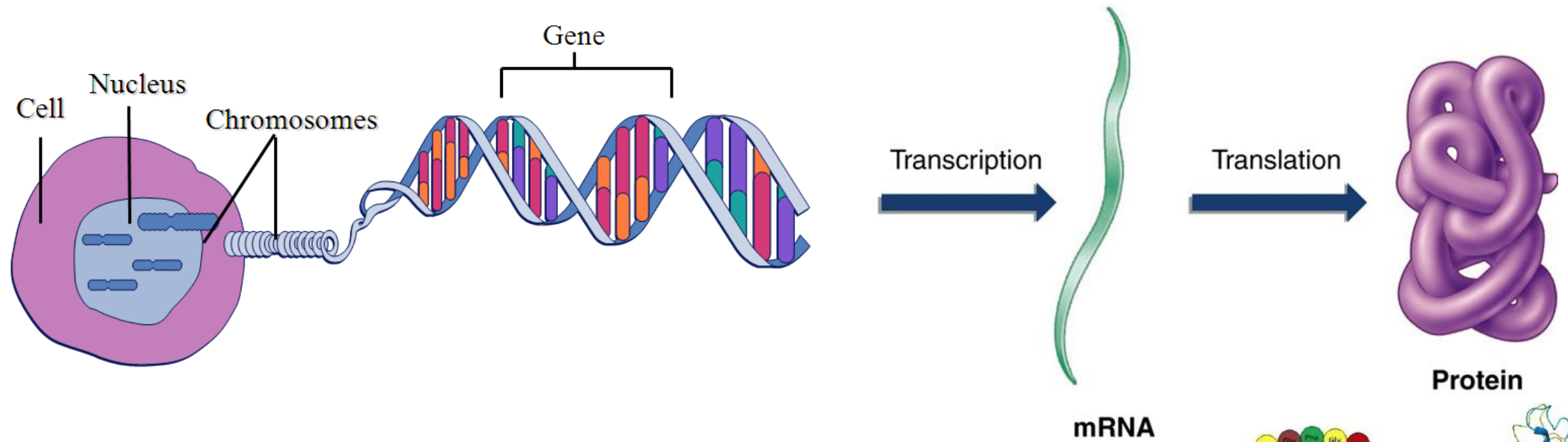


Exon 1

p. (protein) amino acid numbers	1	2	3	4	5	6	7	8	9	10	11
Met	Ala	Asn	Leu	Ala	Ser	Pro	Arg	Phe	Gly	Ser	
.....CAA	ATG	GCC	AAT	CTT	GCT	AGC	CCT	AGA	TTT	GGT	TCT.....
c. (coding) nt numbers	1	4	7	10	13	16	19	22	25	28	31

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 = codon 1 ATG>TTG
 c.13_15delGCT
 (p.Ala5del)
 = codon 5 GCT deletion
 c.16_17delAG
 (p.Ser6ProfsX2)
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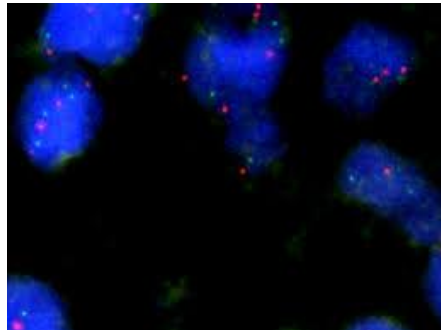
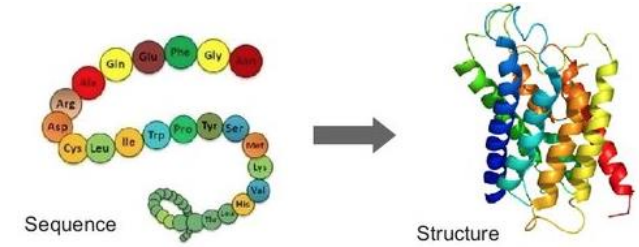


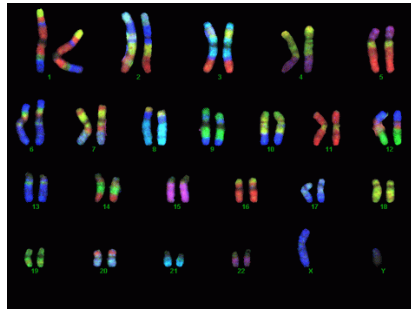
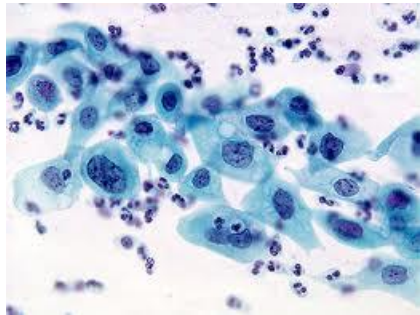
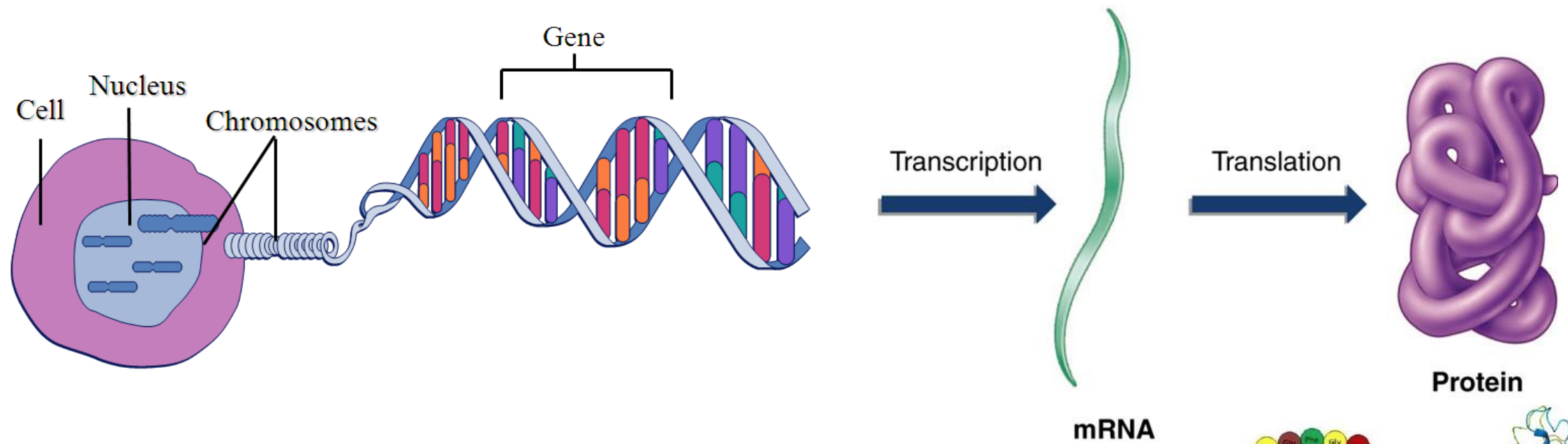


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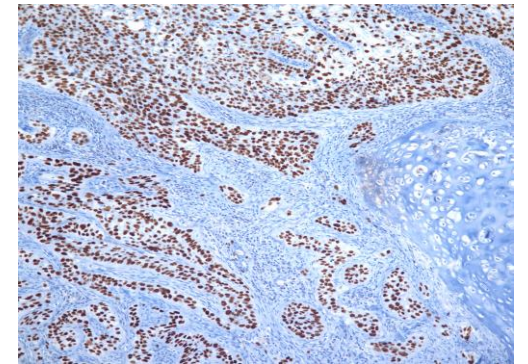
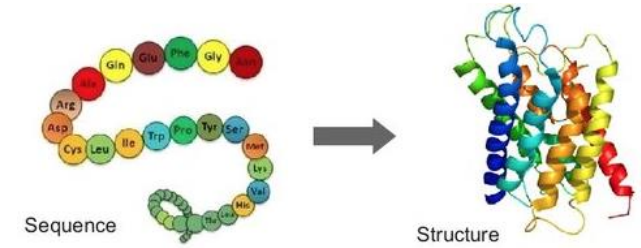
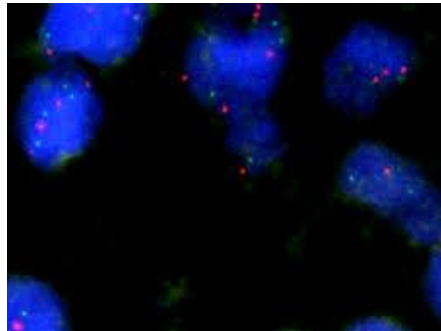


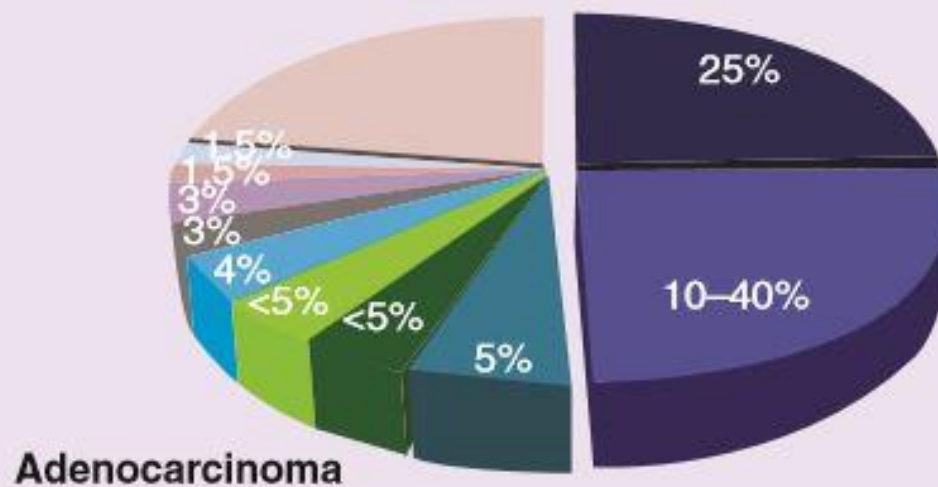


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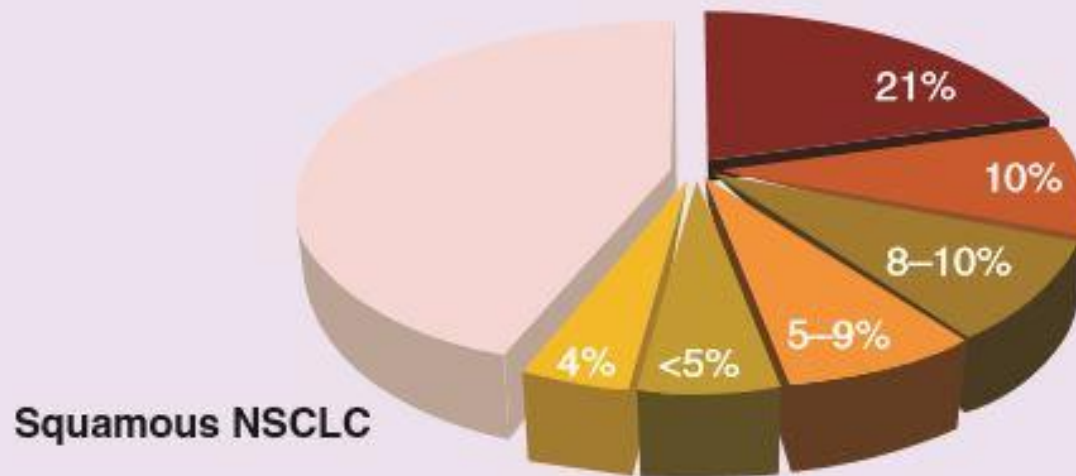
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- *KRAS* mutation
- *EGFR* mutation
- *ALK* rearrangement
- *MET* amplification
- *PIK3CA* mutation
- *HER2* mutation
- *BRAF* mutation
- *NTRK1* rearrangement
- *ROS1* rearrangement
- *RET* rearrangement
- Others or unknown



- *FGFR1* amplification
- *PTEN* mutation
- *PDGFRA* amplification
- *PIK3CA* mutation
- *MET* amplification
- *DDR2* mutation
- Others or unknown

Figure 1. Clinically relevant genetic alterations in adenocarcinoma and squamous non-small-cell lung cancer. <http://www.futuremedicine.com/doi/full/10.2217/fon.14.275>

Begrensninger

- Mengde vev vi mottar
 - Ofte kun marginal mengde tumorvev
 - Kun fraksjon av tumors totale volum blir undersøkt



Isformklipp

10

10



Begrensninger

- Mengde vev vi mottar
 - Ofte kun marginal mengde tumorvev
 - Kun fraksjon av tumors totale volum blir undersøkt
- Dårlig bevart materiale / feil forbehandlet
 - Dårlig morfologi
 - Dårlig DNA og RNA kvalitet

Utfordringer

Faglige

- Gi korrekt diagnose på lite materiale
- Korrekt tolkning av spesialanalyser
 - Ikke alt er sort/hvitt

Økonomisk-politiske

- Kostnader
 - Dyre reagenser (for laboratoriet)
 - Dyr apparatur
 - *Utdatert apparatur*
-Kompliserte innkjøpsrutiner
- Personell
 - Etterutdanning
 - Lite ressurser til kurs etc
 - Opptrening

Utfordringer

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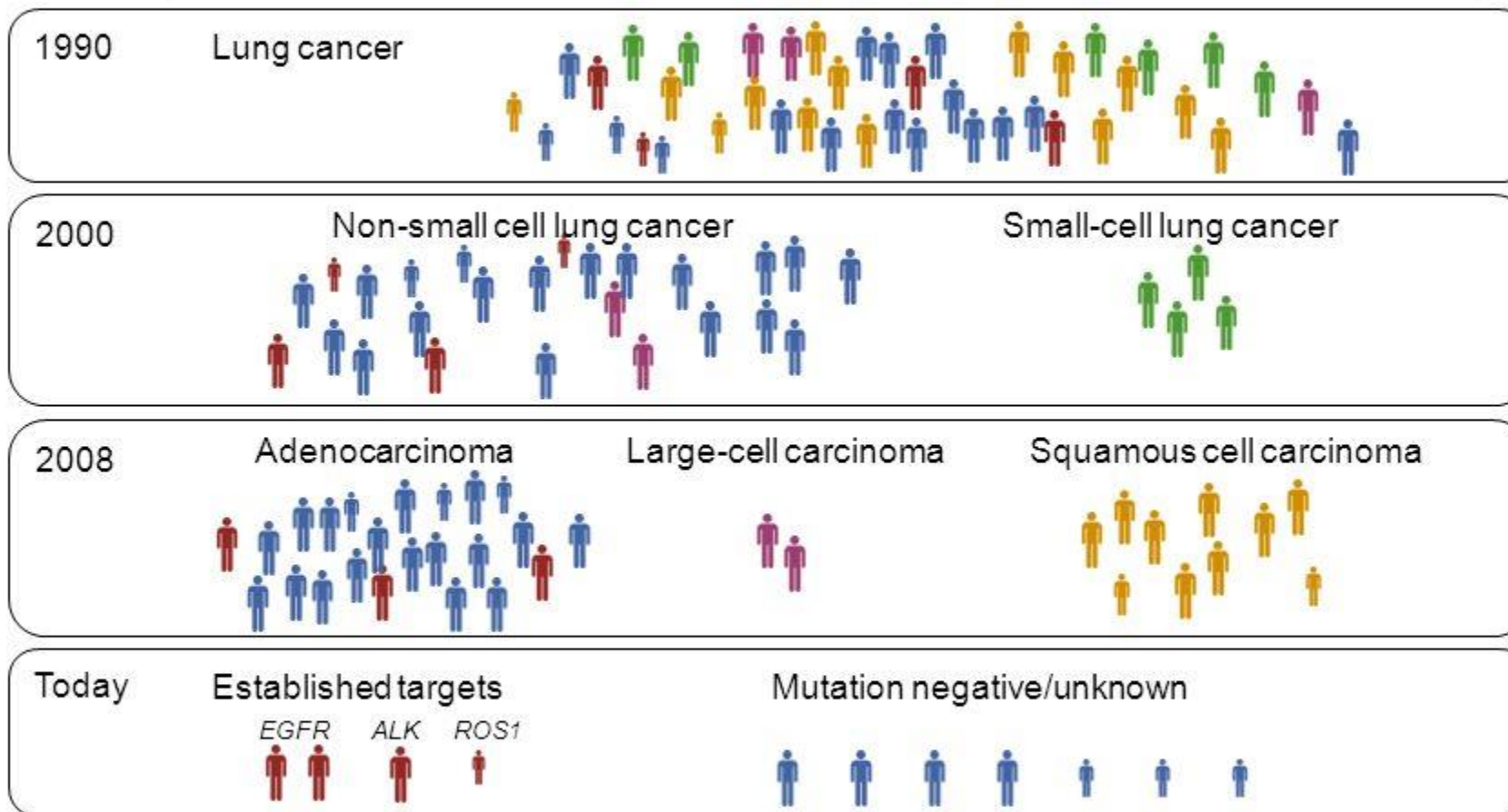
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LOGISTISKE LØP

Patient selection in lung cancer: Evolution over time



Immunotherapy



Adenocarcinoma



Adenocarcinoma and treatable oncogenic alterations



Large cell carcinoma



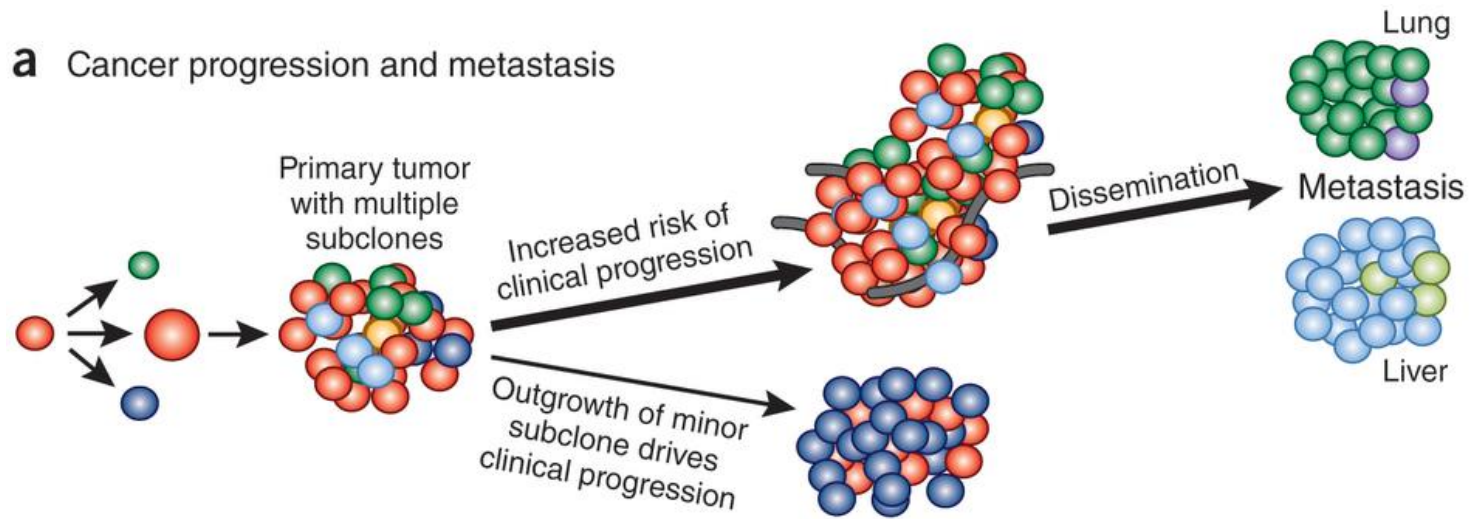
Small-cell lung cancer



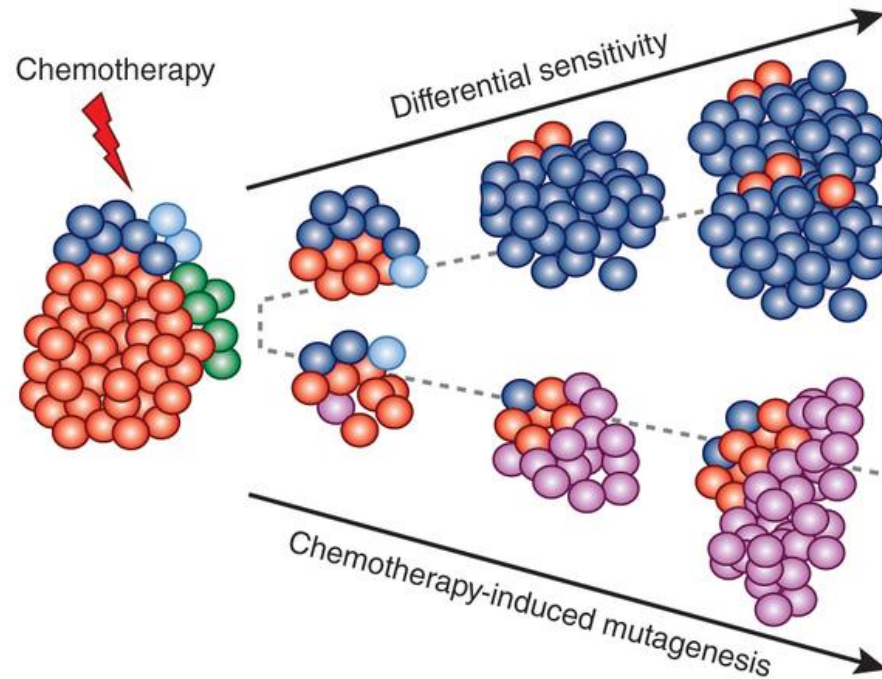
Squamous cell carcinoma



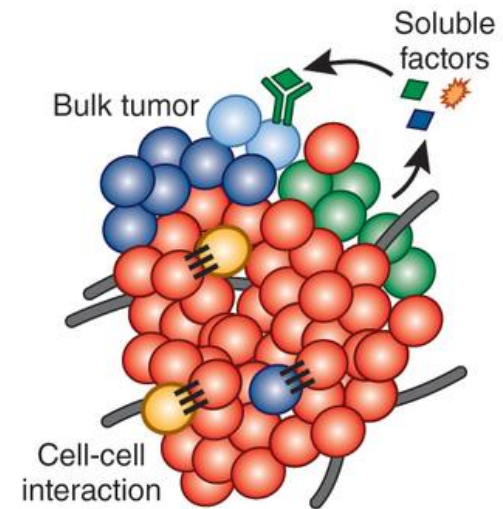
a Cancer progression and metastasis

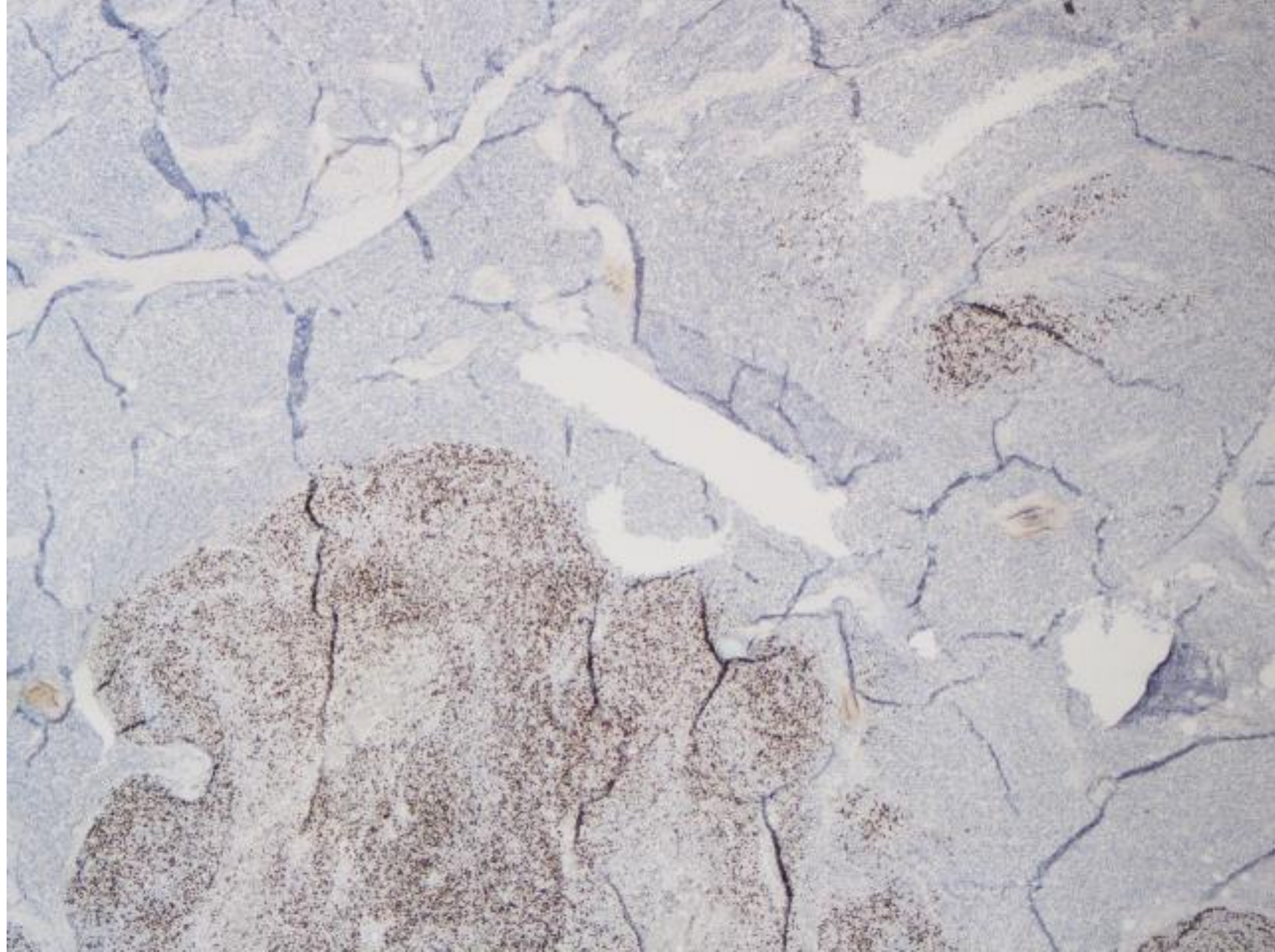


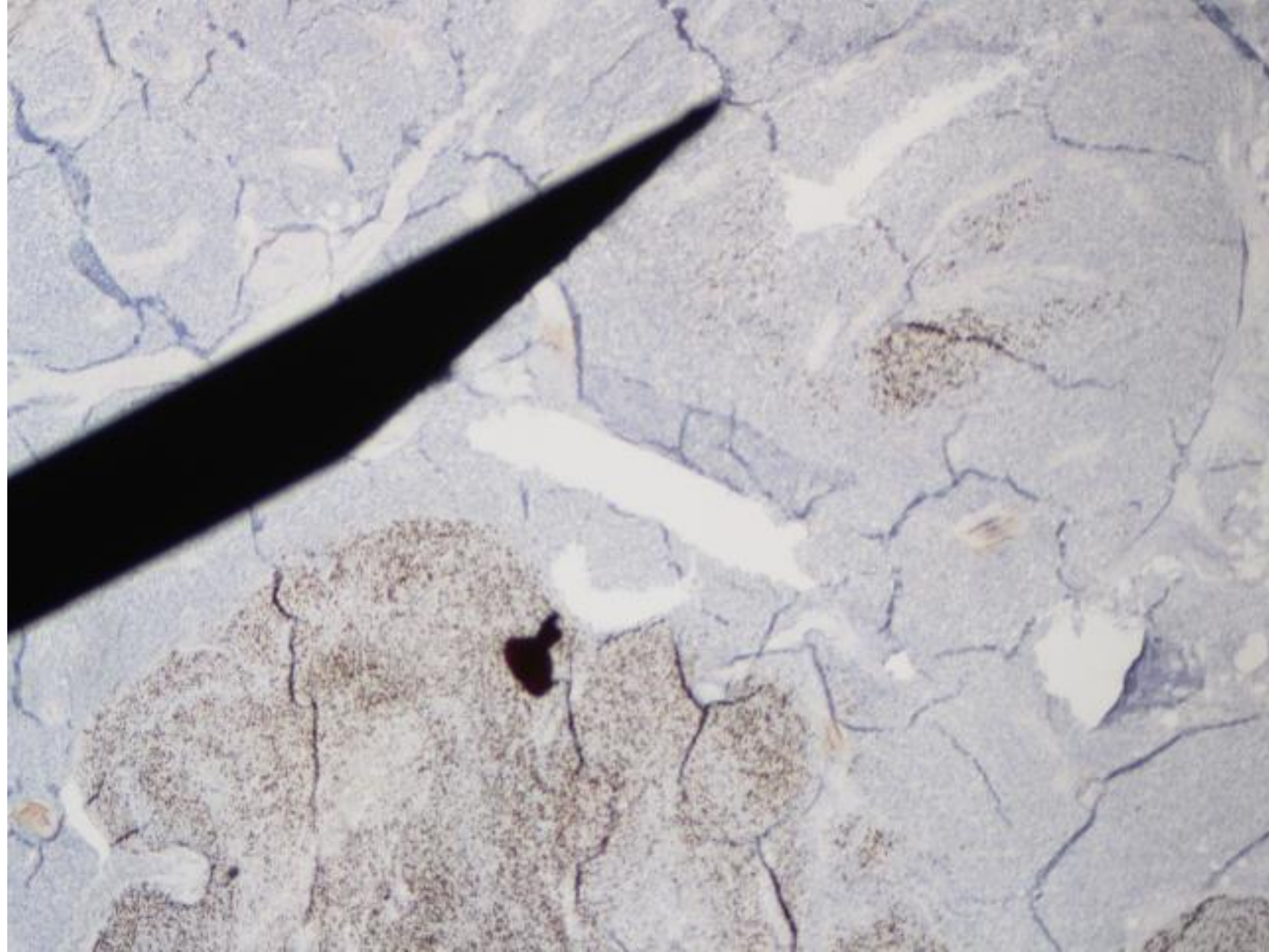
b Response to treatment and clinical resistance

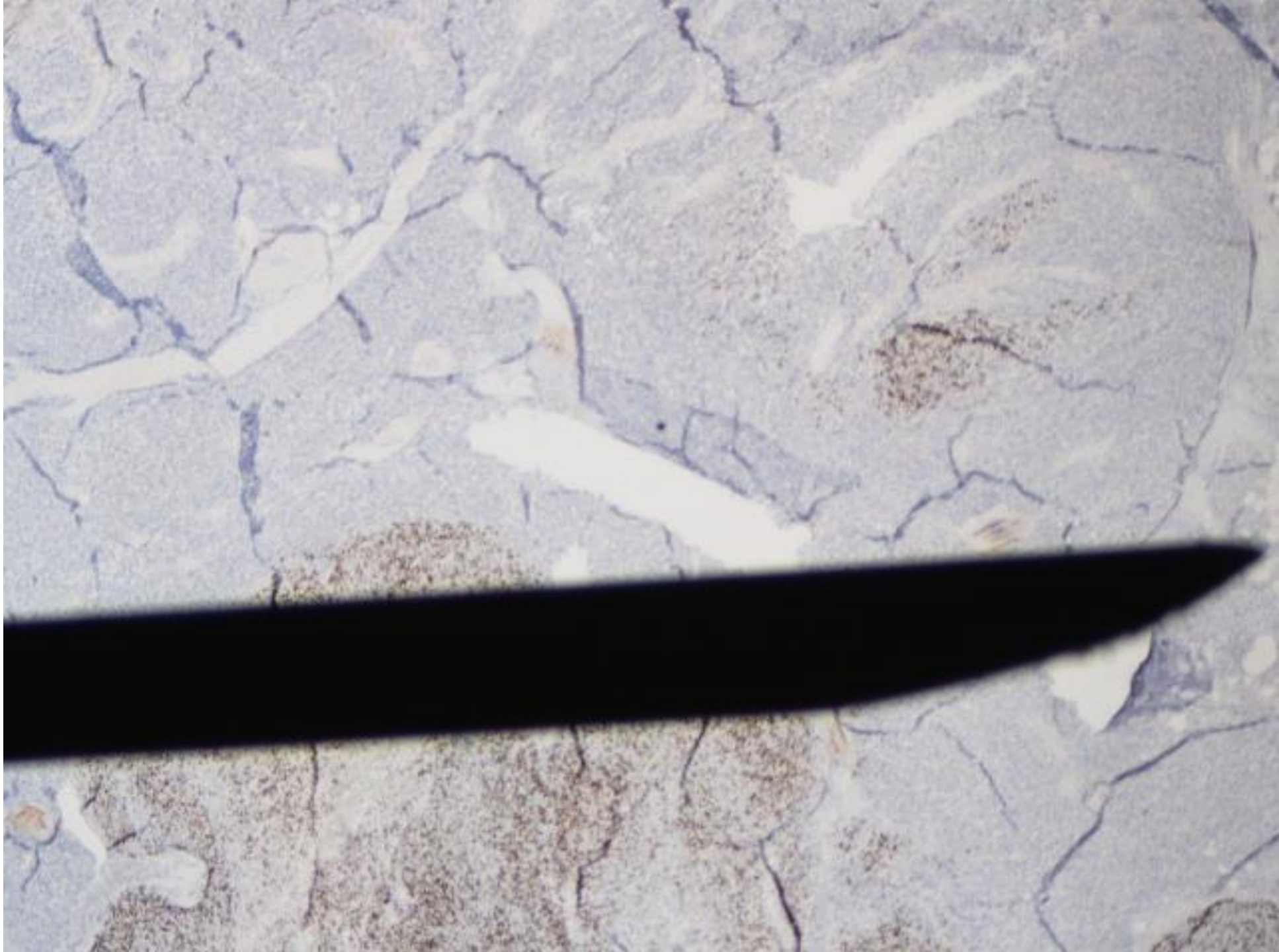


c Biological significance









Hvilke utfordringer gir dette?

- Tilfeldig om tumor blir klassifisert som positiv eller negativ
- Kan ha avgjørende betydning for om en pasient får behandling eller ikke
- Patologen som «kliniker»
 - Skal man jenne resultatet i «pasientfavør»?
 - Hvor skal terskelen for rebiopsring ligge?
 - Hvor liberale skal man være??

Pasientforløp

- 2008: Ikke-småcellet karsinom (utstryk/cytologi)
 - Negativ/uegnet histologisk prøve
- Kjemoterapi og strålebehandling
- 2013: Metastase fra adenokarsinom i bekkenvegg (biopsi)
 - 2 runder med ultralydveilede biopsier nødvendig
- EGFR og ALK rekvireres i ettertid når svaret foreligger
 - Innstøpt materiale er oppbrukt på immunhistokjemi for å verifisere lunge som origo
 - Ikke mer vev i blokken

- Prøven (utstryk) fra 2008 tas frem igjen
 - Prepareres for EGFR analyse (relativt omstendig prosess)
 - EGFR er negativ

- Kliniker venter fortsatt på ALK svaret
- Da dette tar tid rekvireres i mellomtiden BRAF
 - Bevart ekstrahert DNA etter EGFR analysen i prøven fra 2008 benyttes
 - BRAF er negativ

- ALK svaret etterlyses
 - Det formidles at det ikke er mer tumorvev igjen til denne analysen....

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Ny biopsi og ALK og ROS rekvireres

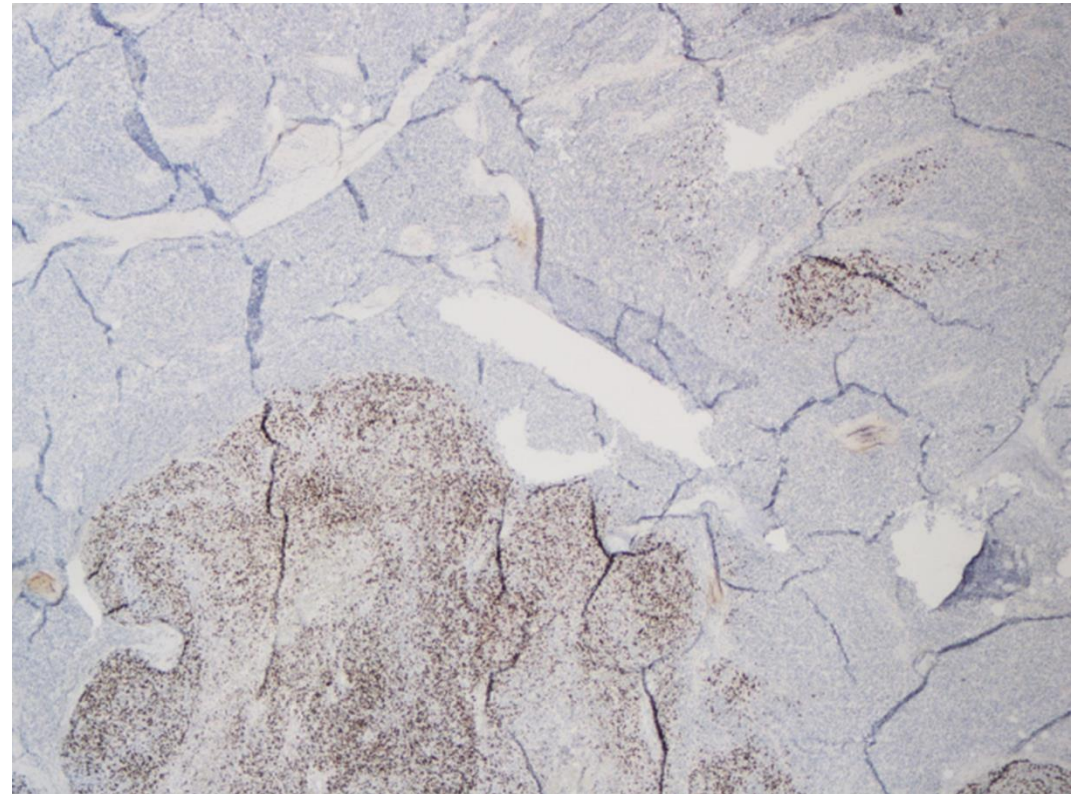
Negative



- Pas til privat sykehus for immunterapi
 - God effekt
- Fortsatt i live
- Ønsker nå analyse mhp PD-L1
 - Behandling i offentlig regi

- Pasienten får derfor tatt en 4. biopsi for å få utført analysen
 - PD-L1 er negativ

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Sammenfatning

Muligheter

- Mulig med brede analyser på tumorvevet
- Retrospektive analyser på arkivert materiale går fint
 - Versus rebiopsi
- Når DNA først er isolert kan dette brukes til flere analyser, eg. EGFR og BRAF

Utfordringer

- Minimere unødvendige undersøkelser
- Gode logistiske løsninger vedrørende prøveflyt
- Alle analyser initialt eller suksessive rekvireringer?
- Synliggjøre de diagnostiske og analytiske utfordringer
- Valg av riktig metode
 - Enkeltanalyser vs store screeningpaneler?
- Økonomi og ressurser

Takk for oppmerksomheten