

# Sitolojik Tanı Örneklerinin Moleküler Analizinden Öğrendiklerimiz

Dr. Zafer KÜÇÜKODACI

GATA Haydarpaşa Eğitim Hastanesi  
Patoloji Servisi

21. Ulusal Patoloji Kongresi Kasım 2011 İzmir

INTEGRATION LEADING TO FULL DIAGNOSTIC, PROGNOSTIC AND THERAPEUTIC OPINION

MORPHO-MOLECULAR INTEGRATION

CLINICO-PATHOLOGICAL INTEGRATION

Pulmonary pathology

Urological  
Pathology

CNS Pathology

Lymphoreticular  
Pathology

Gynaecological  
Pathology

Gastrointestinal  
Pathology

Soft Tissue Pathology

Breast  
Pathology

I  
M  
M  
U  
N  
O  
H  
I  
S  
T  
O  
C  
H  
E  
M  
I  
S  
T  
R  
Y

E  
L  
E  
C  
T  
R  
O  
N  
M  
I  
C  
R  
O  
S  
C  
O  
P  
Y

Clinical History  
and  
Clinical  
Presentation

Other  
Laboratory  
Investigations

Diagnostic  
Imaging

*EGFR* Mutations

Various  
Chromosomal  
Abnormalities (BC)

1p 19q LOH (Gliomas)

B- and T-cell receptor  
gene rearrangements  
Multiple translocations

HPV Subtype Identification

*KRAS/BRAF* mutations (CRC)  
MSI analysis  
*c-kit* mutation (GIST)  
*Her-2/neu* amplification (GC)

Multiple translocations

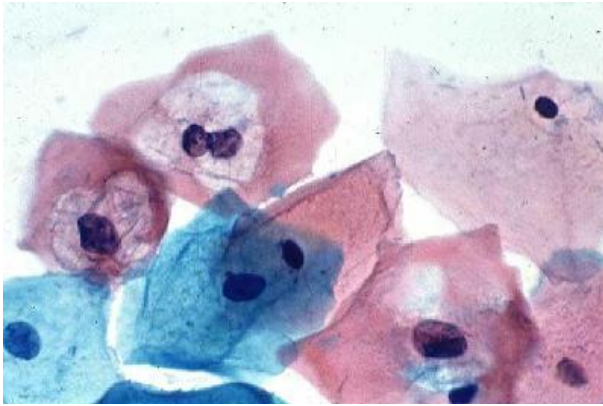
*Her-2/neu* amplification  
*TOP 2A* amplification  
Multiple gene amplification

**FINAL  
PATHOLOGICAL  
OPINION  
(DIAGNOSTIC &  
THERAPEUTIC)**

# JINEKOLOJİK SİTOLOJİ

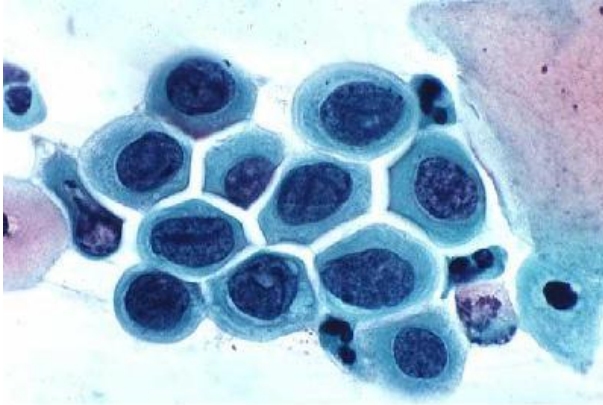
- Serviks kanserinin etiyolojik ajanı
- HPV aşısının geliştirilmiş olması

\*

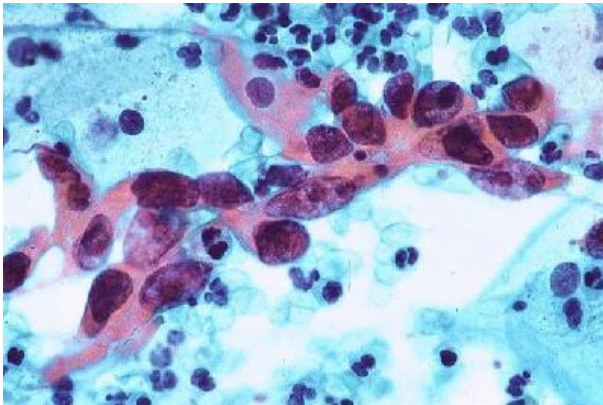


%83

\*\*

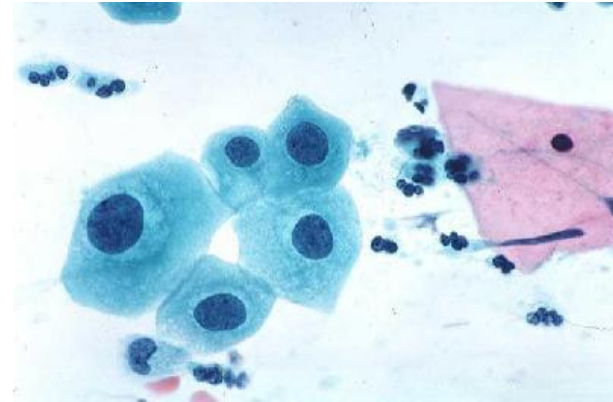


%91

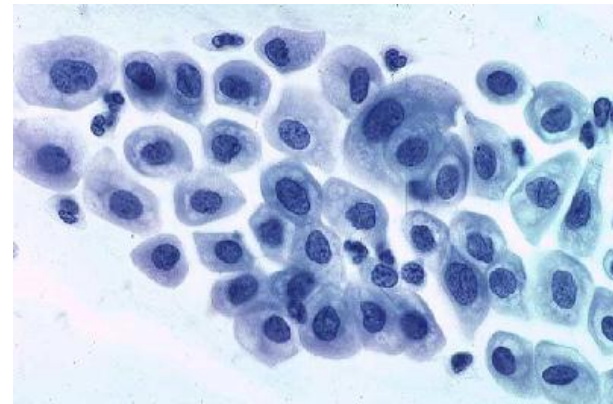


%99.7

## Skvamöz epitelyal hücre anormalliği



%56



%81

\* NCI Bethesda System Website Atlas

\*\* Sherman et al. ALTS Trial. J. Natl Cancer Inst, 2002

Zuna et al. Cancer Cytopathol, 2005

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Vol.90, Cervix Cancer Screening . IARC Pres. 2005

# HPV-DNA'sının Saptanması ve Genotiplendirilmesi

- İn situ hibridizasyon
- Southern blot/dot spot hibridizasyon
- Nükleik asit amplifikasyon metodları
  - Sinyal amplifikasyon sistemleri
  - Hedef amplifikasyon sistemleri
    - Geniş spektrum PCR
    - Tip spesifik PCR

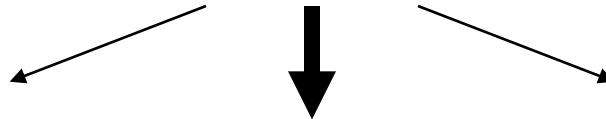
DNA EKSTRAKSİYONU



Tarama  
(Geniş spektrum PCR)



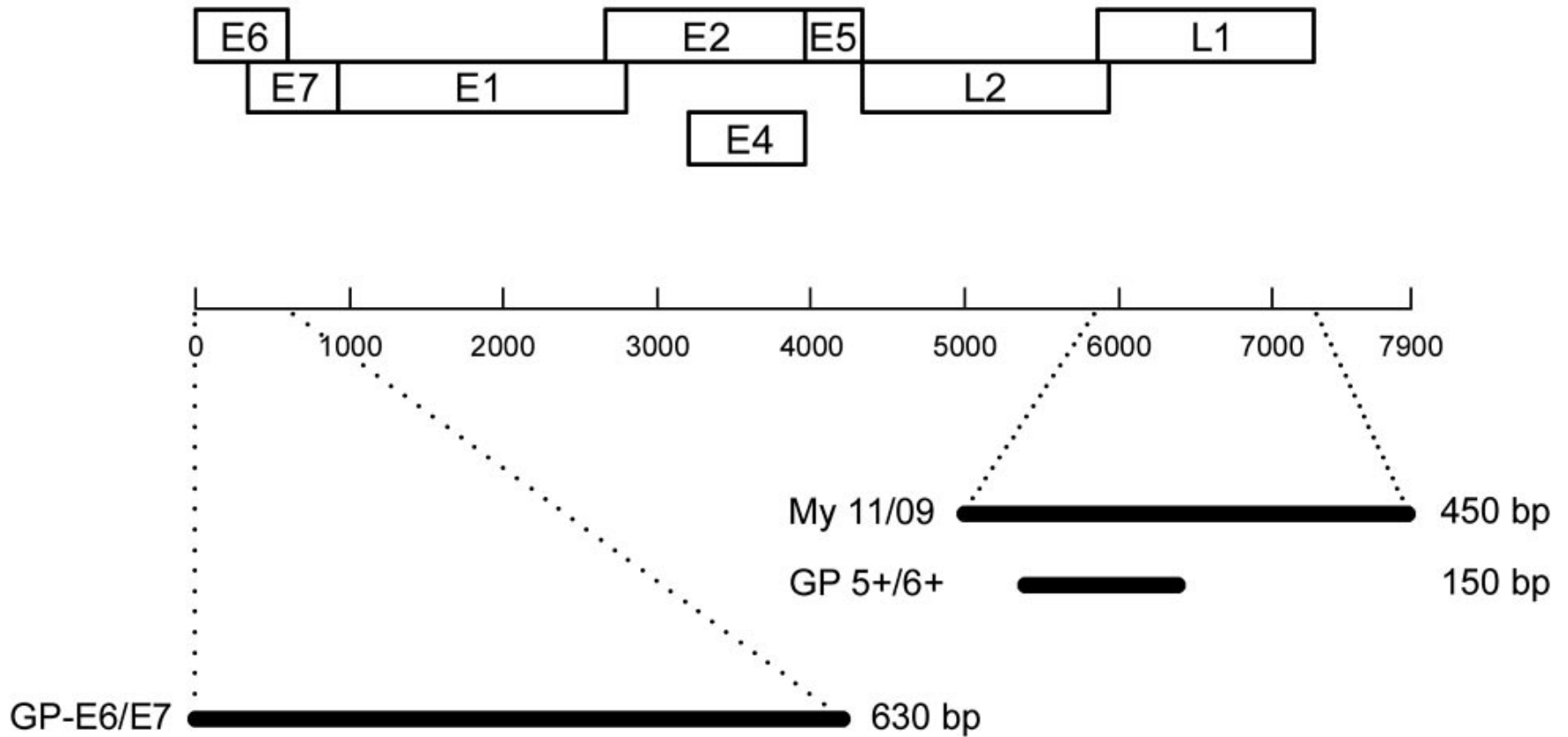
Tipleme



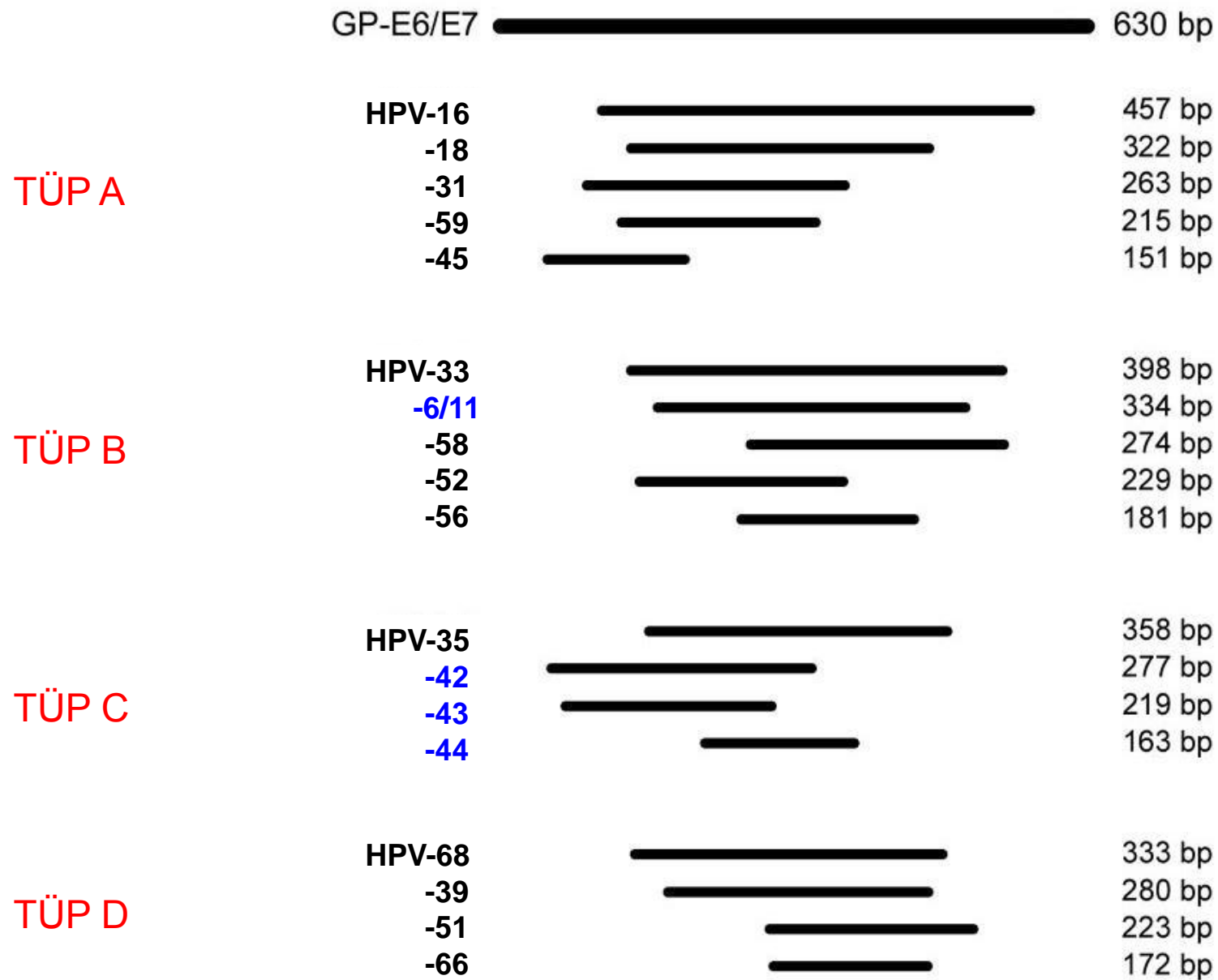
Hibridizasyon

MPCR

Sekans

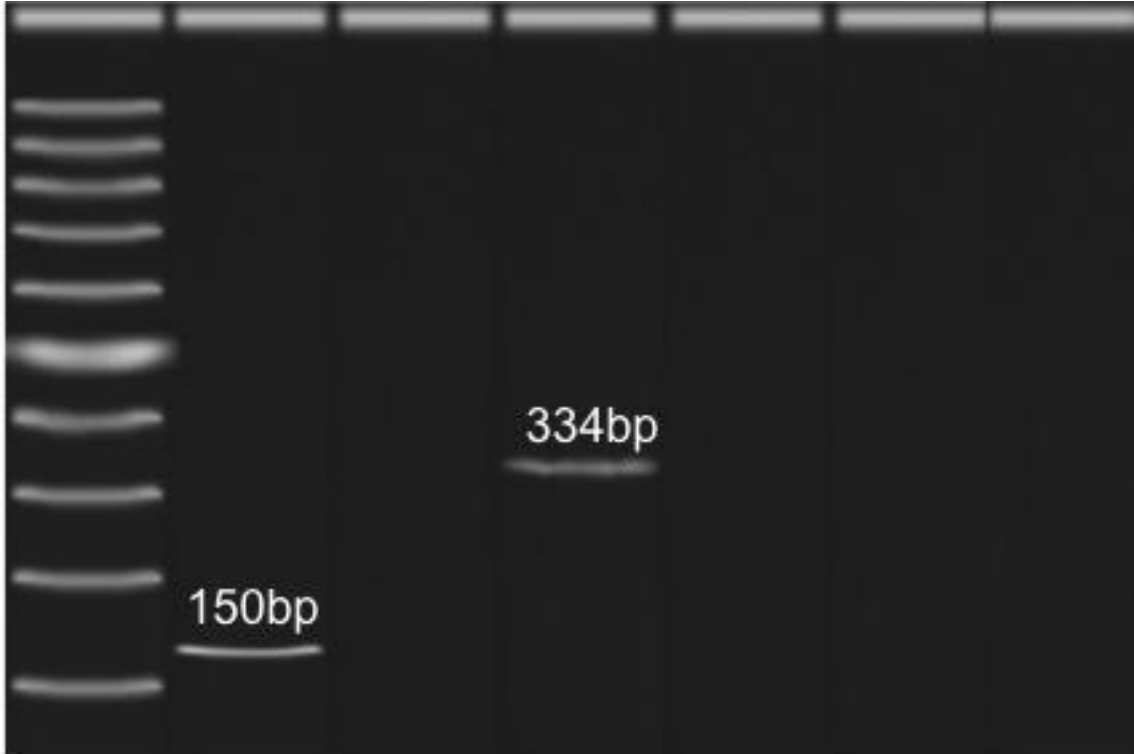
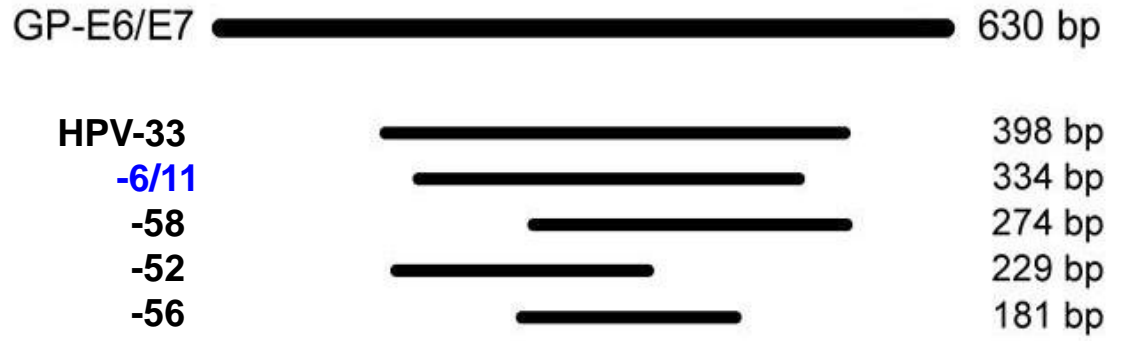


*Sotlar et al. Detection and Typing of Human Papillomavirus by E6 Nested Multiplex PCR. J. Clin. Microbiol; 2004: 3176–3184.*





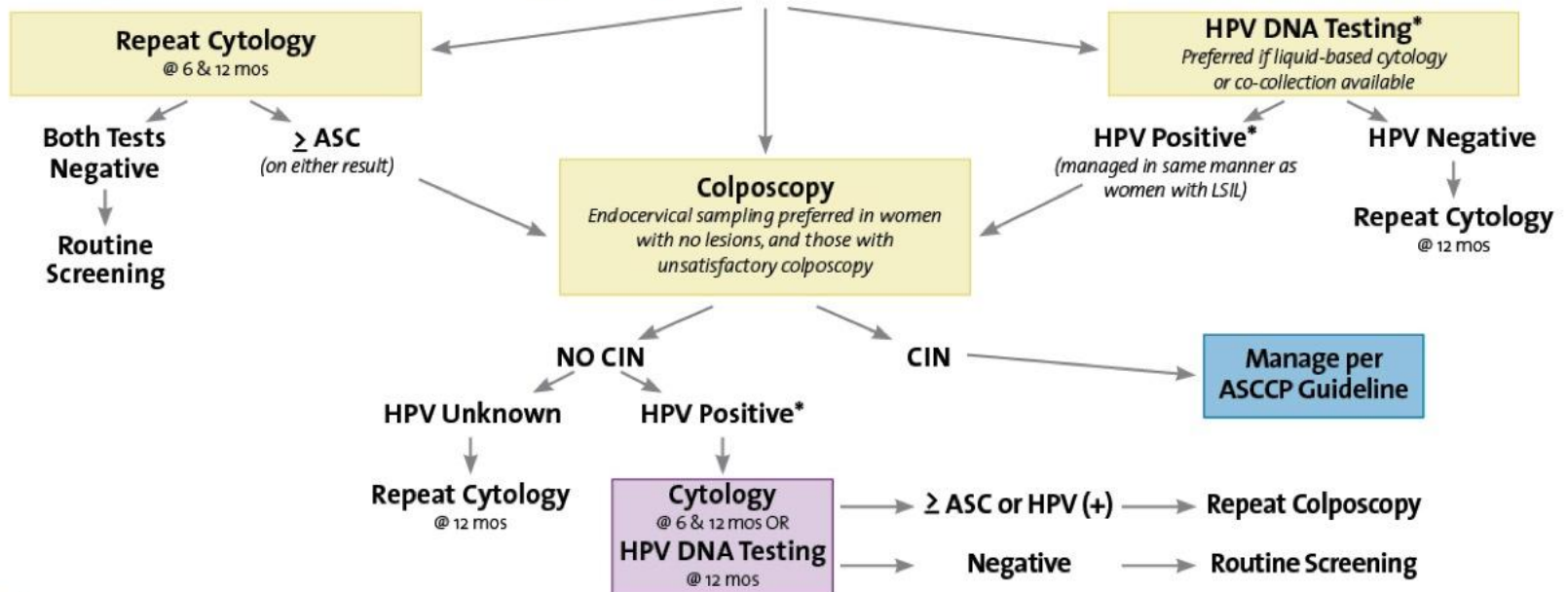
MY9/11 & GP5/GP6

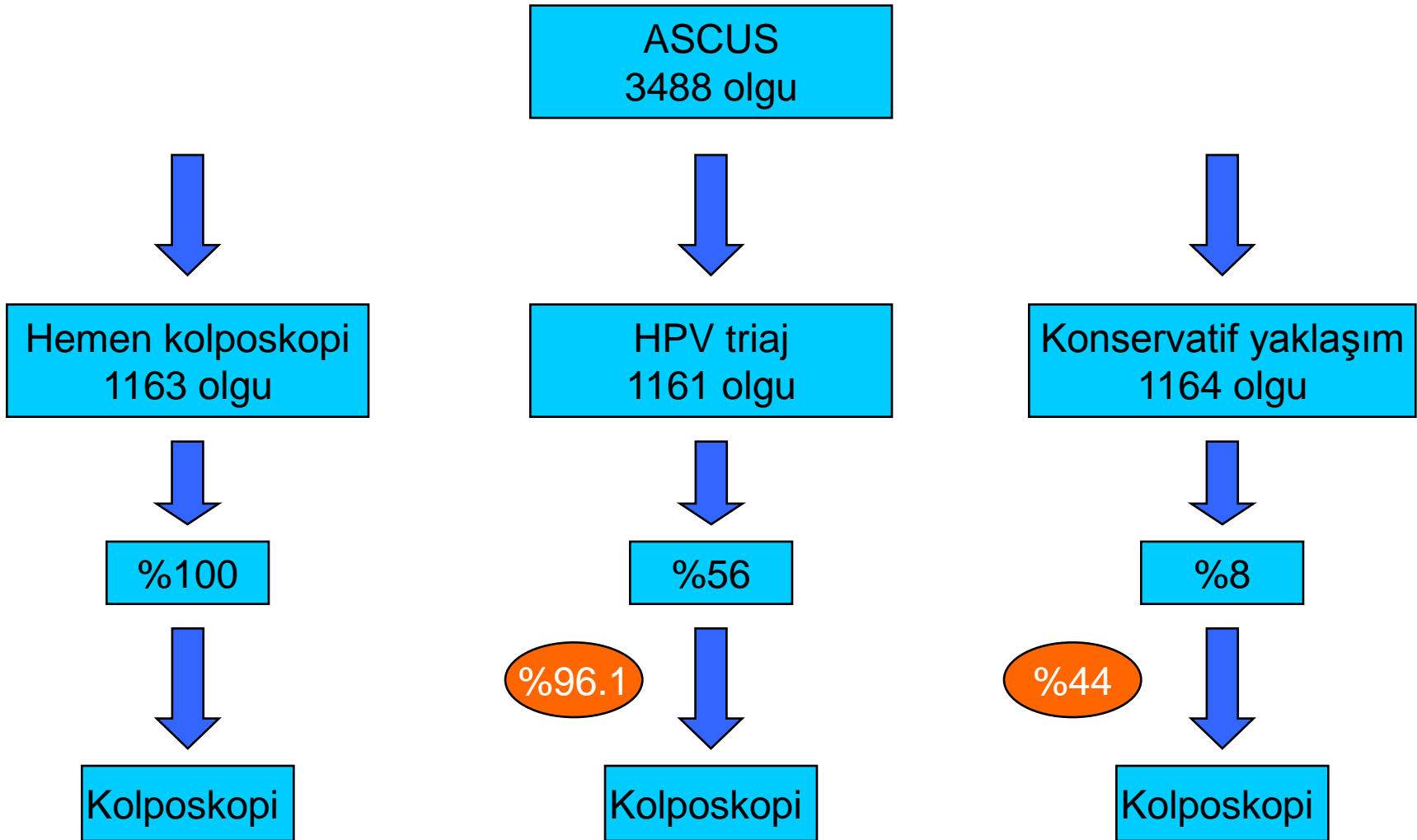


# HPV-HR

- Sitolojik ASC-US tanısı alan hastalarda kolposkopi gerekliliğini belirlemek için
- 30 yaş ve üstü kadınlarda, yüksek riskli HPV tiplerinin olup olmadığı göstermek için servikal sitoloji ile birlikte kullanılabilir

## Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US)





*Schiffman M, Solomon D. Findings to Date From the ASCUS-LSIL Triage Study (ALTS). Arch Pathol Lab Med.2003(127);946-949.*

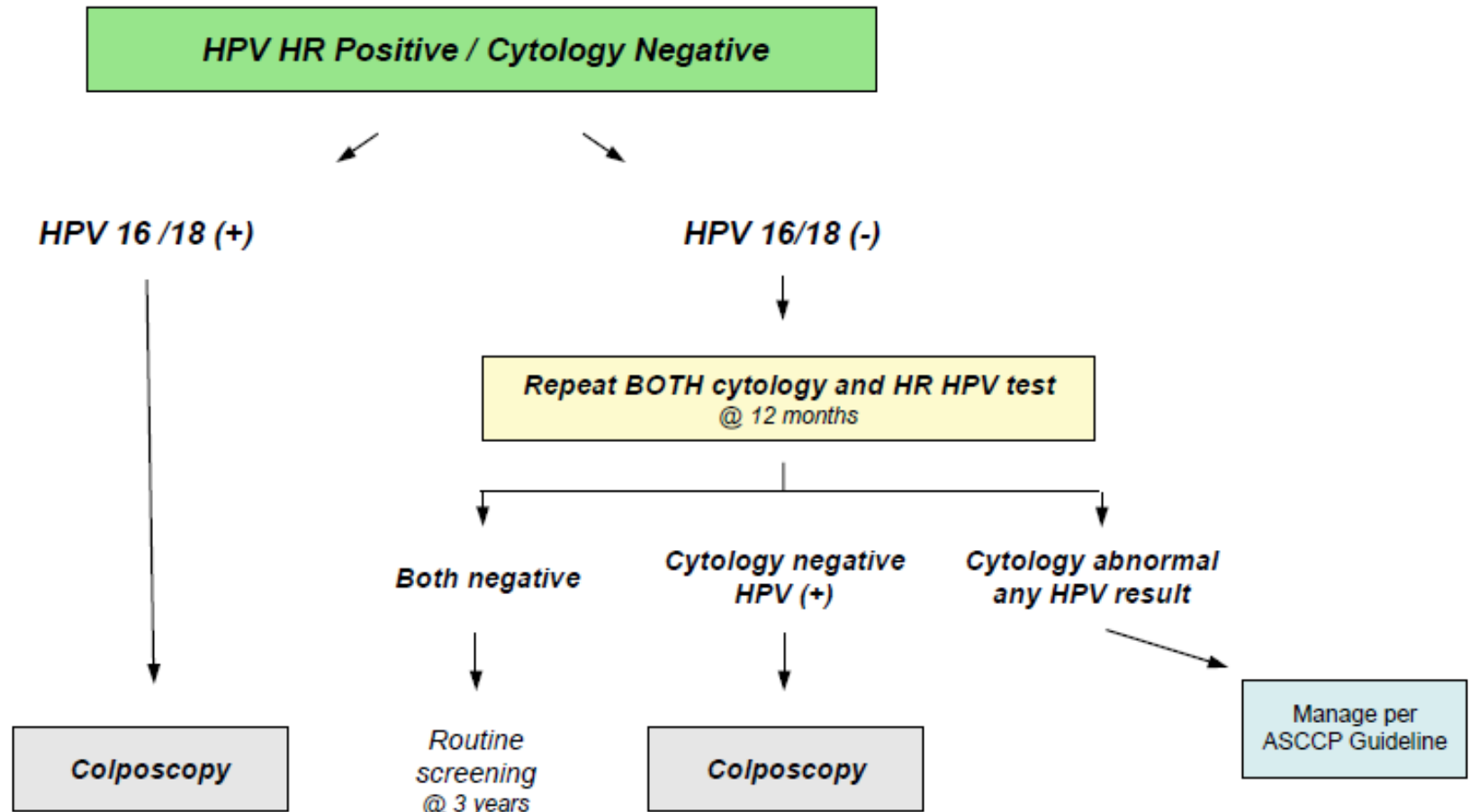
# HPV 16/18 GENOTİPLEME

1. 30 yaş ve üstü kadınlarda, HPV HR testine ilave olarak yüksek riskli HPV 16 ve 18 tiplerinin olup olmadığını göstermek için servikal sitoloji ile kombine olarak kullanılabilir.

2. Servikal sitoloji sonucu ASC-US olan hastalarda HPV HR testine ilave olarak HPV 16 ve 18 tiplerinin olup olmadığını göstermek için kullanılır.

- Genotipleme testleri 30 yaştan genç kadınlar için uygun değildir.
- Genotipleme, anormal Pap sonuçları olan kadınlarda takip şeklini değiştirmeyeceği için uygun değildir.

# Use of HPV Genotyping to Manage HPV HR \* Positive / Cytology Negative Women 30 Years and Older



# HPV Genotiplenmesi Klinik Güncelleme

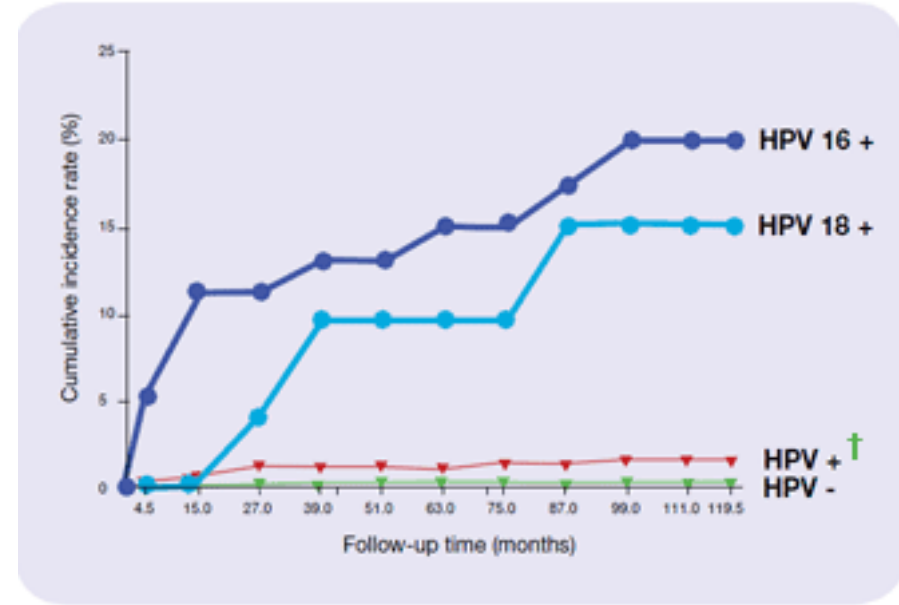
## Ulusal kanser enstitüsü çalışmalarında

- HPV tip 16 ve 18'li kadınlarda, 10 yılı aşkın Pap test negatifliğine rağmen, CIN3 gelişme riski yaklaşık %20'dir ve bu kadınlarda kolposkopi faydalı olabilir
- Özellikle 30 yaş altı kadınlarda, çoğu HPV 16/18 infeksiyonları geriler (bu kadınların yaklaşık % 20'sinde yüksek riskli HPV infeksiyonu vardır)

HPV 16 pozitif, sitolojisi negatif kadınların 10 yıllık takiplerinde CIN3+ %21

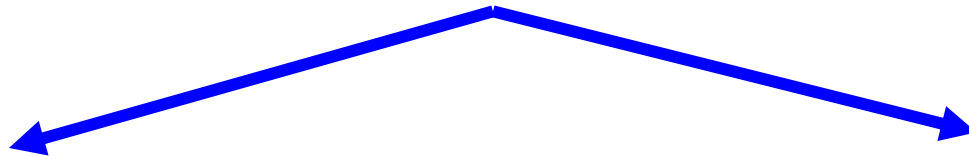
HPV 18 pozitif, sitolojisi negatif kadınların 10 yıllık takiplerinde CIN3+ %18

Diğer HR HPV'ler pozitif, sitolojisi negatif kadınların 10 yıllık takiplerinde CIN3+ %1.5

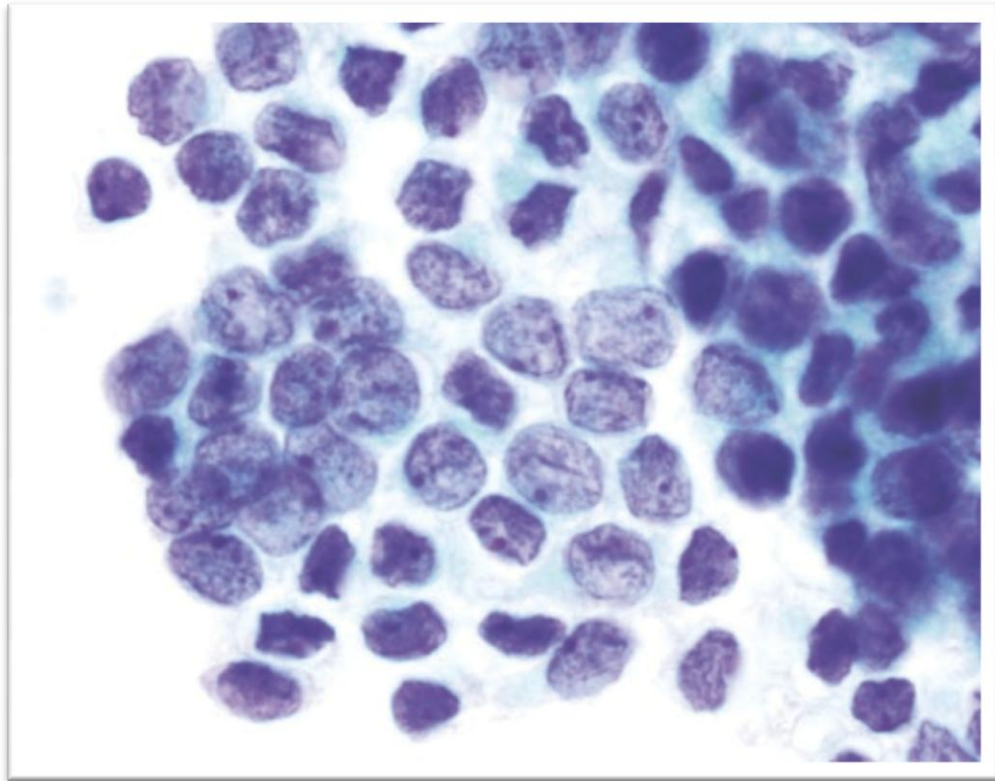


Khan, et al., Journal of the National Cancer Institute 2005  
† Non HPV 16/18 high-risk types





LBC



# Tissue Overview for Thyroid

Sub Tissue : NS

Histology : Adenoma-nodule-goitre, Carcinoma, Chronic thyroiditis, Other

The genes displayed below are associated with samples that have the tissue type you have selected.

## » Top 17 Genes

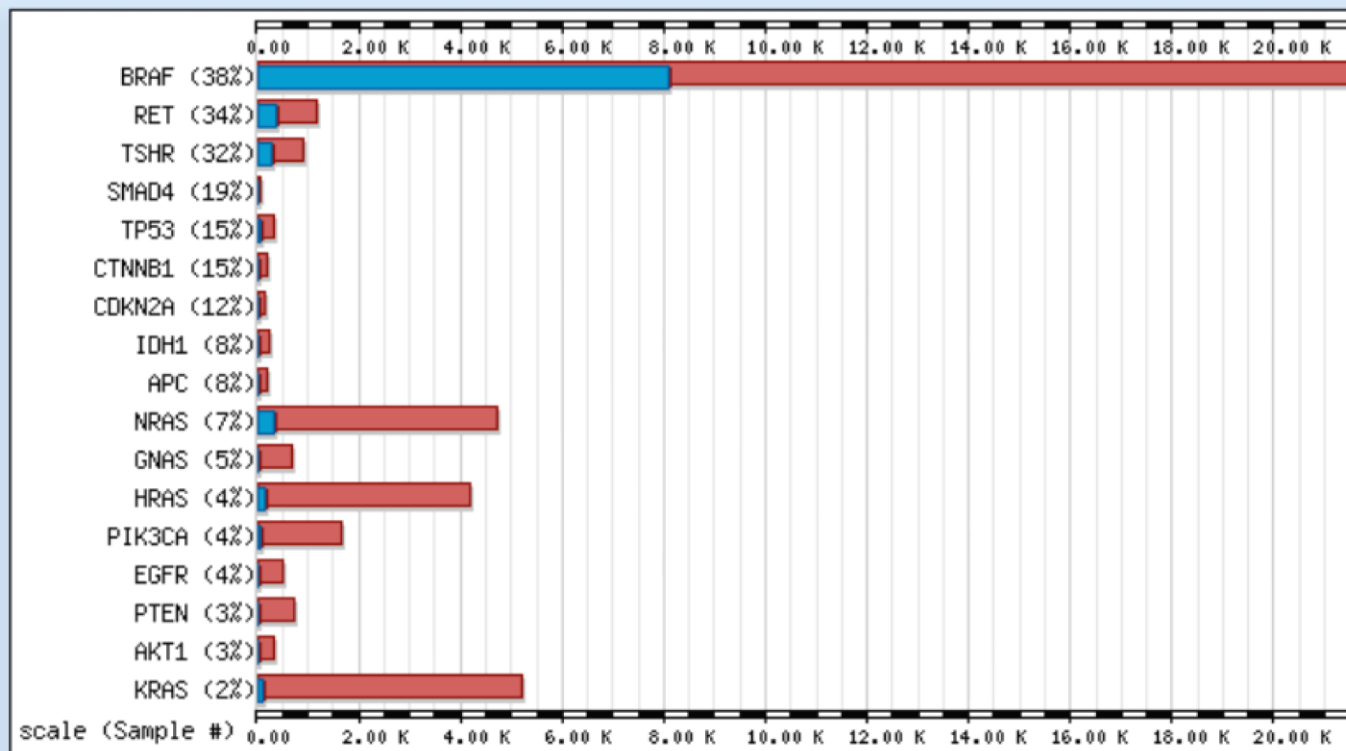


Image Key: Samples with mutations All samples

This bar graph highlights the most significantly mutated genes from the [Cancer Gene Census](#)

[www.sanger.ac.uk/genetics/CGP/cosmic/](http://www.sanger.ac.uk/genetics/CGP/cosmic/)

# Tissue Overview for Thyroid

Sub Tissue : NS

Histology : Adenoma-nodule-goitre, Chronic thyroiditis, Other

The genes displayed below are associated with samples that have the tissue type you have selected.

## » Top 7 Genes

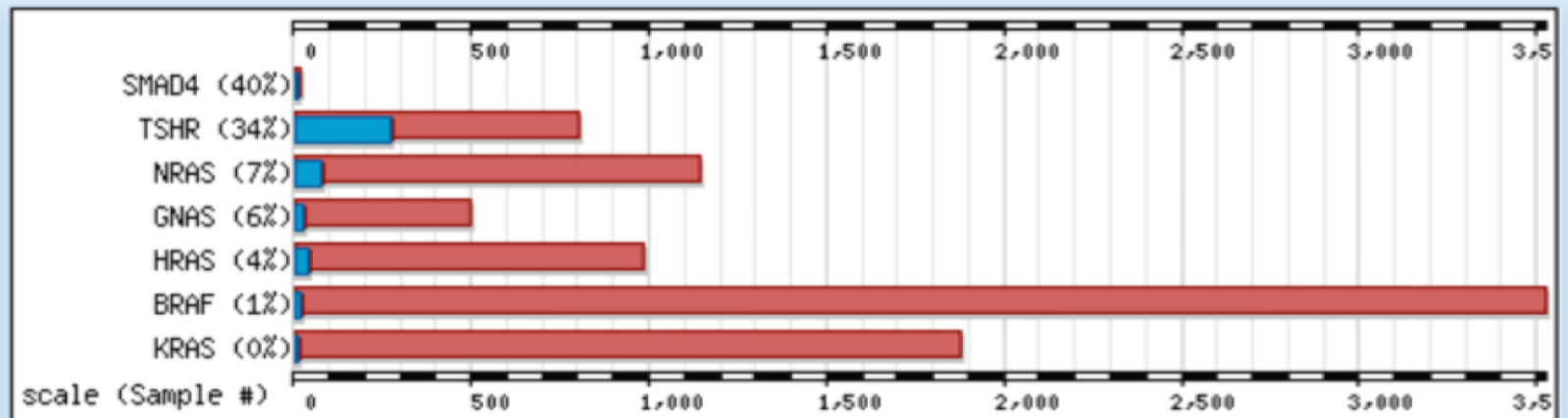


Image Key: Samples with mutations All samples

This bar graph highlights the most significantly mutated genes from the [Cancer Gene Census](#)

To include all genes, please click - Redraw

# Distribution of somatic mutations in BRAF

Export

Zoom Out

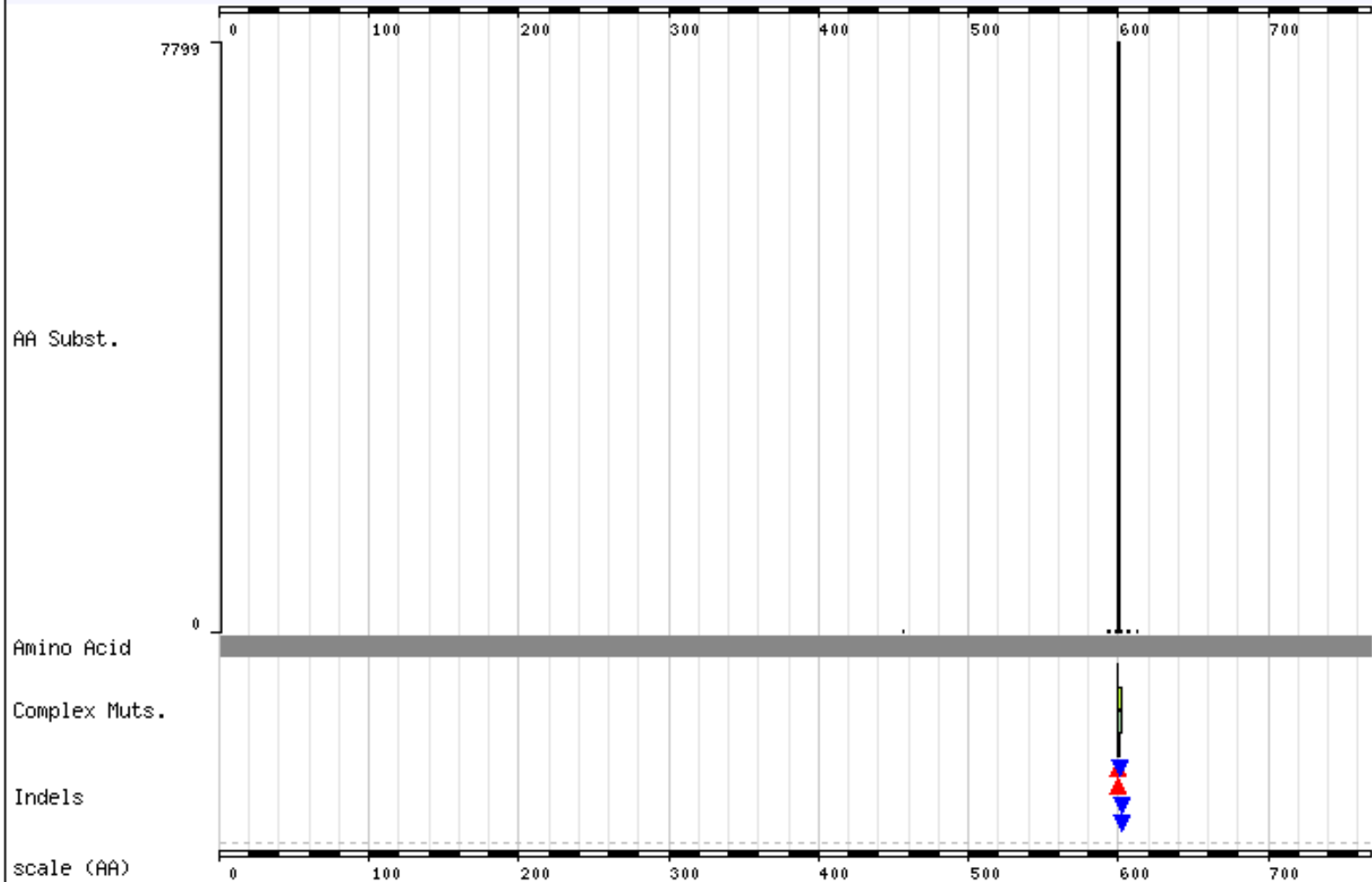
Switch View

References

Summary

Tissue View

BRAF



Navigation

Gene: BRAF



AA

1

to

767

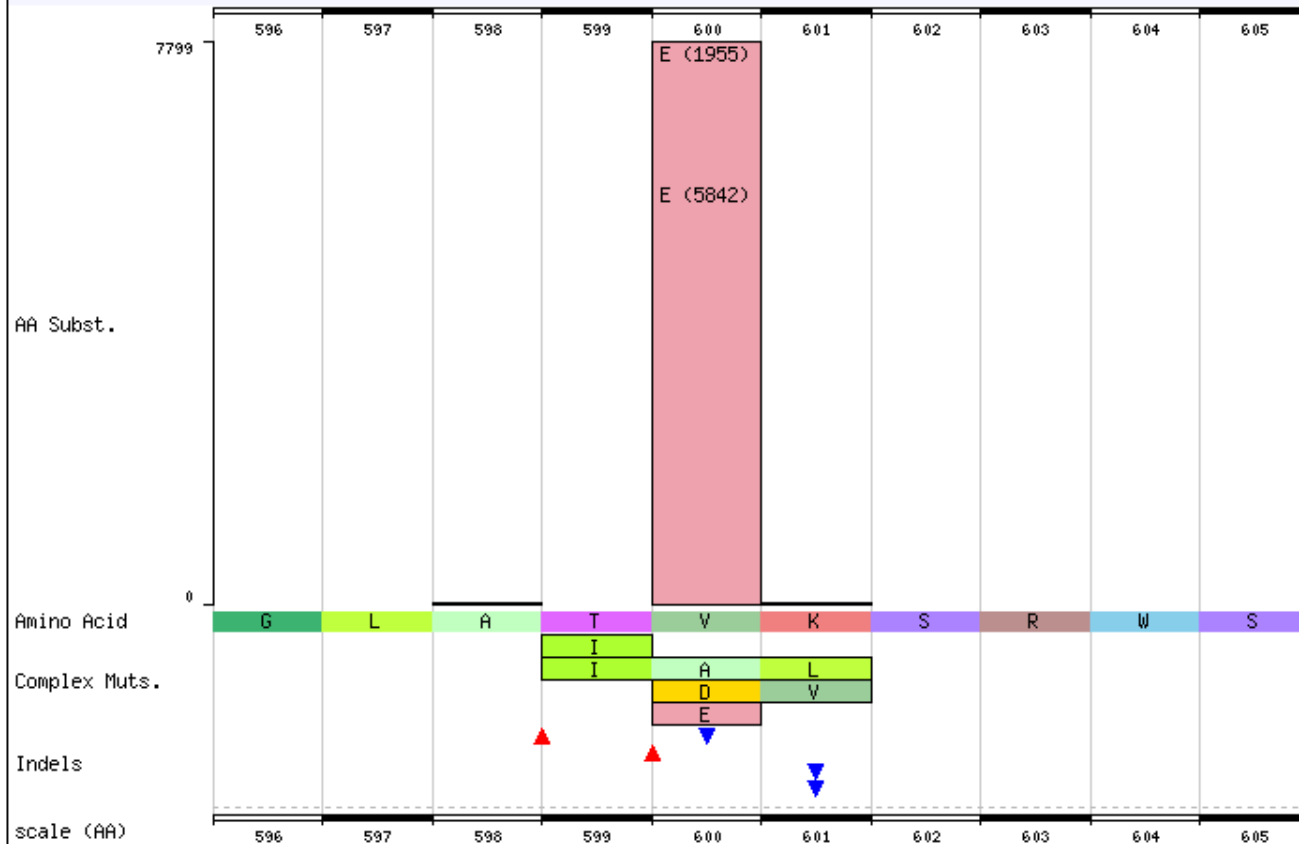
Display

Sequence Type:  cDNA  Amino Acid

# Distribution of somatic mutations in BRAF

[Export](#)
[Zoom Out](#)
[Switch View](#)
[References](#)
[Summary](#)
[Tissue View](#)

BRAF



Navigation

Gene: BRAF

AA

596

to 605

Display

Sequence Type:  cDNA  Amino Acid

## Details for BRAF

Primary Tissue

Histology

Sub Histology

Unique Mutated Samples

% Mutated

Total Unique Samples

Mutation Data

[thyroid](#)

[carcinoma](#)

[papillary carcinoma](#)

[7798](#)

48%

[16376](#)

[More Details](#)

Totals

[7798](#)

48%

[16376](#)

[More Details](#)

# Distribution of somatic mutations in BRAF

Export

Zoom Out

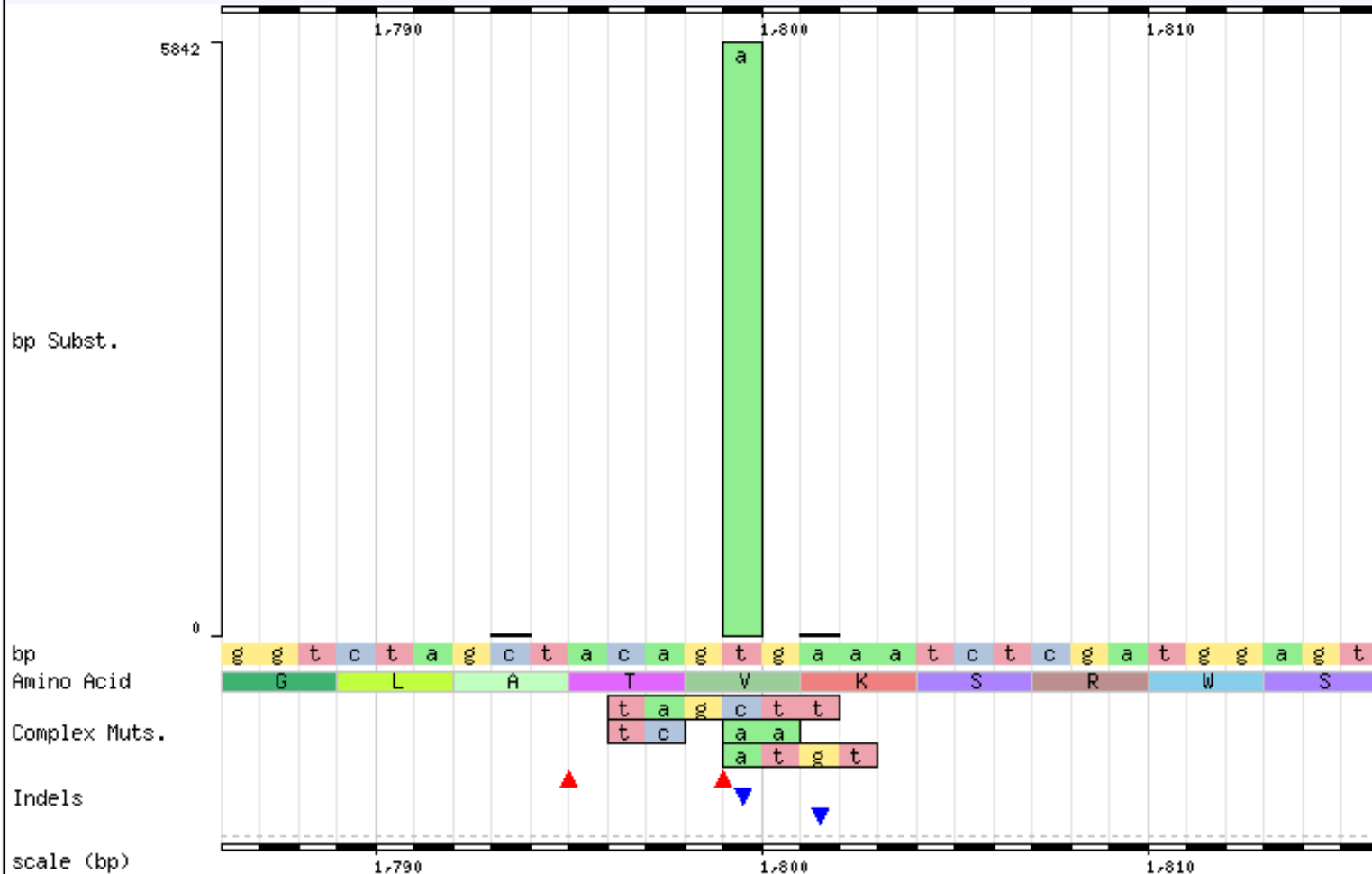
Switch View

References

Summary

Tissue View

BRAF



Navigation

Gene: BRAF

bp

1786

to

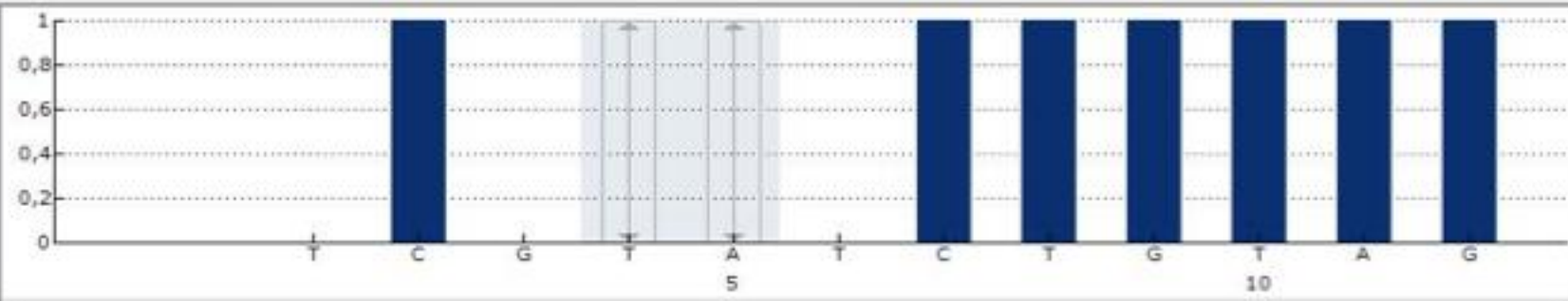
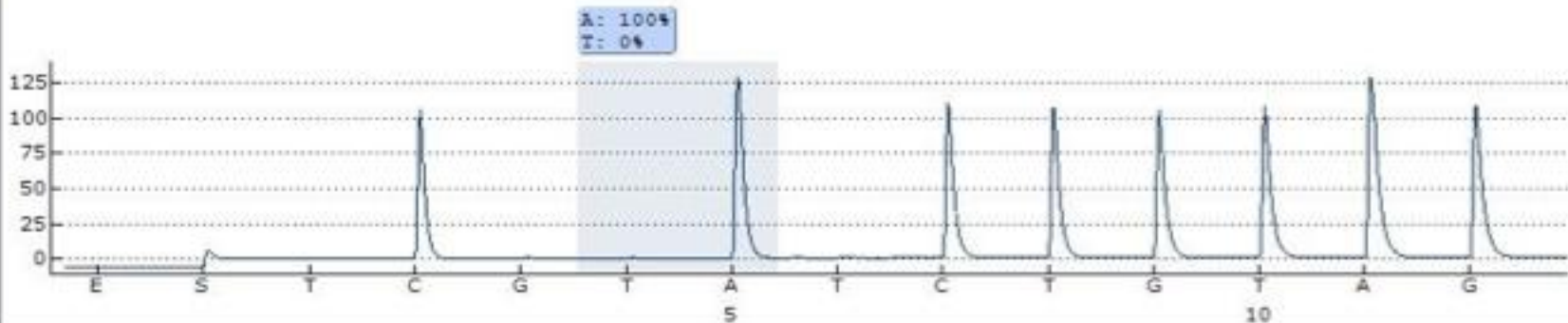
1815

Display

Sequence Type:  cDNA  Amino Acid

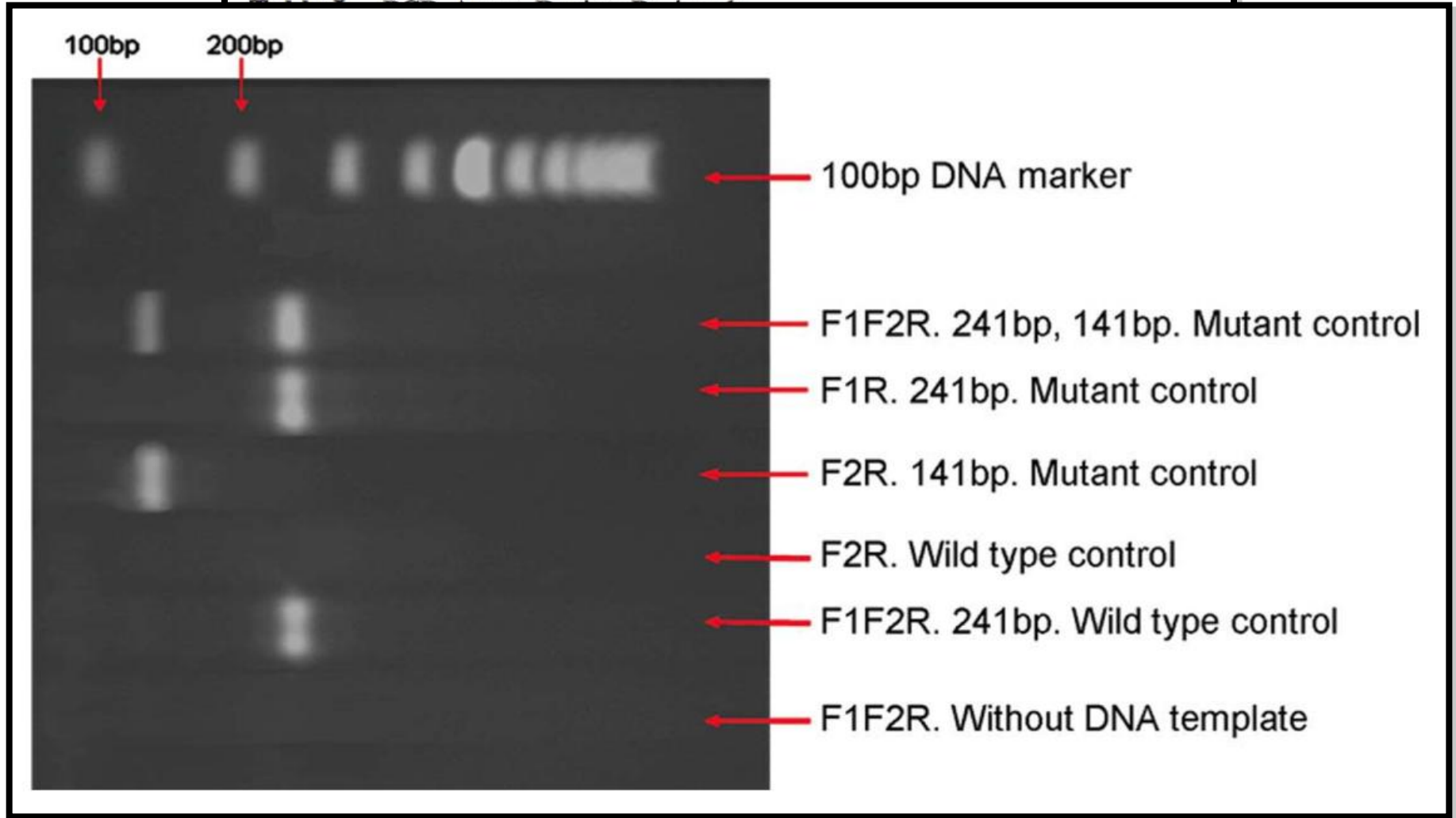
|   |                  |                  |                    |                    |                |                |  |  |
|---|------------------|------------------|--------------------|--------------------|----------------|----------------|--|--|
| B | EGFR del19<br>1E | EGFR del19<br>2E | BRAF 464-469<br>3B | BRAF 464-469<br>4B | BRAF 600<br>3B | BRAF 600<br>4B |  |  |
| C |                  |                  |                    |                    |                |                |  |  |

B6 CWCTGTAGC





# IN-HOUSE PCR ASSAY FOR BRAF T1799A



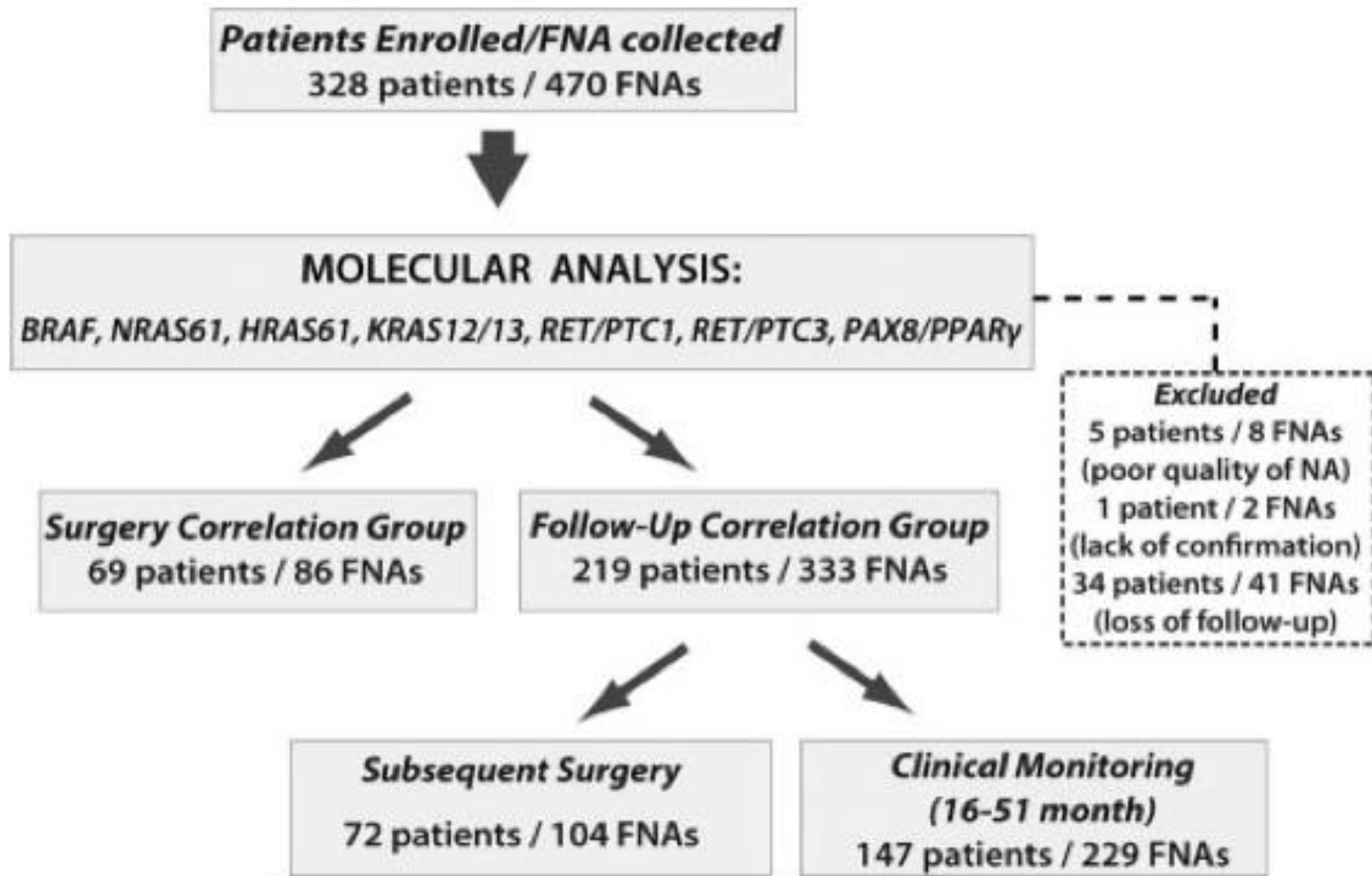
Kucukodaci Z, Akar E, Haholu A, Baloglu H. A Valuable Adjunct To FNA Diagnosis Of Papillary Thyroid Carcinoma: In-House PCR Assay For BRAF T1799a (V600E). *Diagnostic Cytopathology* 2010;39(6):424-427

## **Molecular Testing for Mutations in Improving the Fine-Needle Aspiration Diagnosis of Thyroid Nodules**

Yuri E. Nikiforov, David L. Steward, Toni M. Robinson-Smith, Bryan R. Haugen, Joshua P. Klopper, Zhaowen Zhu, James A. Fagin, Mercedes Falciglia, Katherine Weber, and Marina N. Nikiforova

# Cerrahi uygulanan 69 hastadan alınan 86 İİAB örneklerinin

- Sitolojik tanısı MYP: 22 örnek
- Sitolojik tanısı belirsiz: 52 örnek
- Sitolojik tanısı MYN: 12 örnek

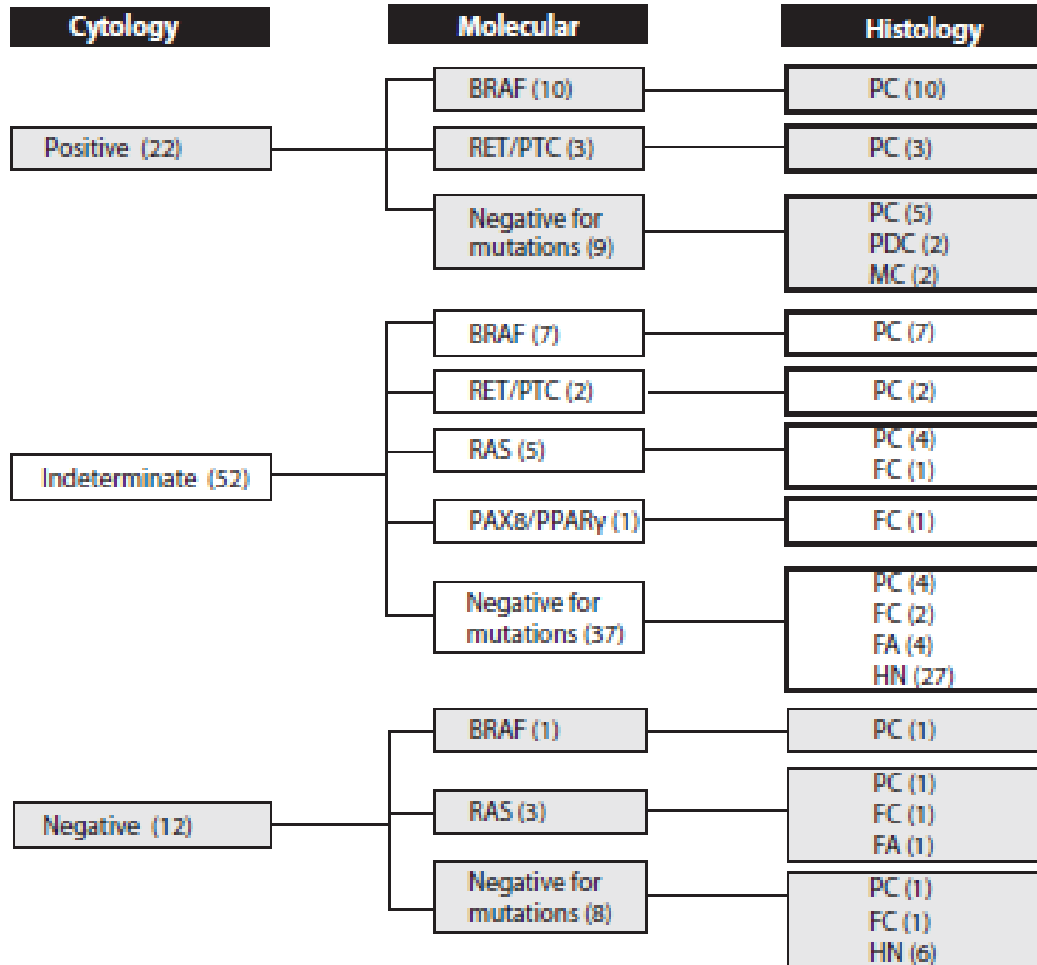


**FIG. 1.** Schematic representation of the study design. NA, Nucleic acids.

# Tiroid İİAB Mutasyonlar

- 86 örneğin 32 tanesinde mutasyon
- BRAF V600E mutasyonu en sık mutasyon
  - BRAF pozitif 18 örneğin tamamı papiller karsinoma
- RAS ikinci sıklıkta saptanan mutasyon (NRAS61, HRAS61)
  - RAS pozitiflerin 5'i Papiller karsinoma folliküler varyant
  - 2'si folliküler karsinoma
  - *1'i folliküler adenoma (HRAS61)*
- RET/PTC
  - 5 pozitif örneğin tamamı papiller karsinoma
- PAX8/PPAR $\gamma$ 
  - 1 pozitif örnek folliküler karsinoma

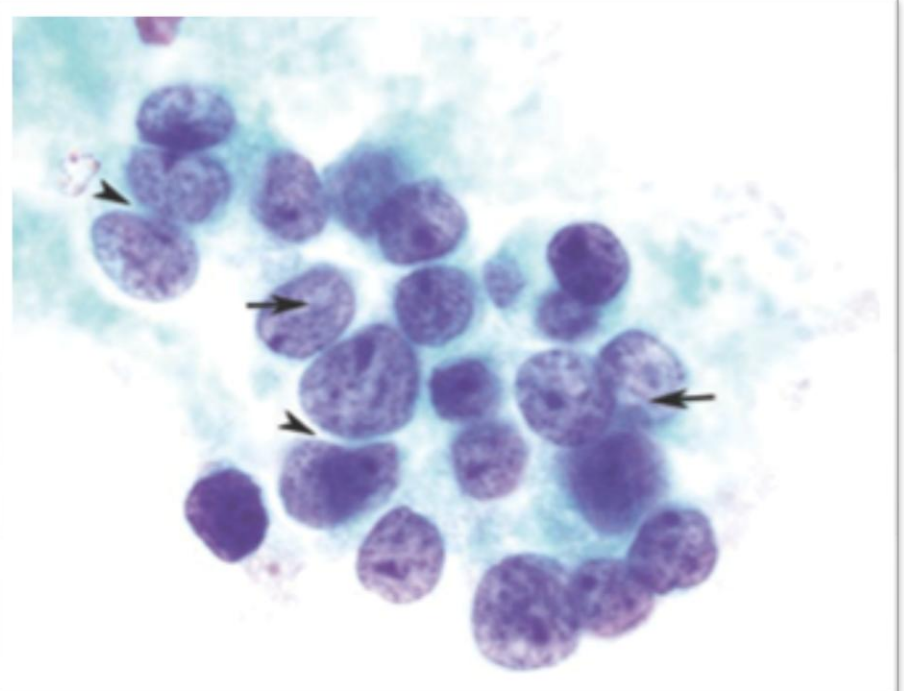
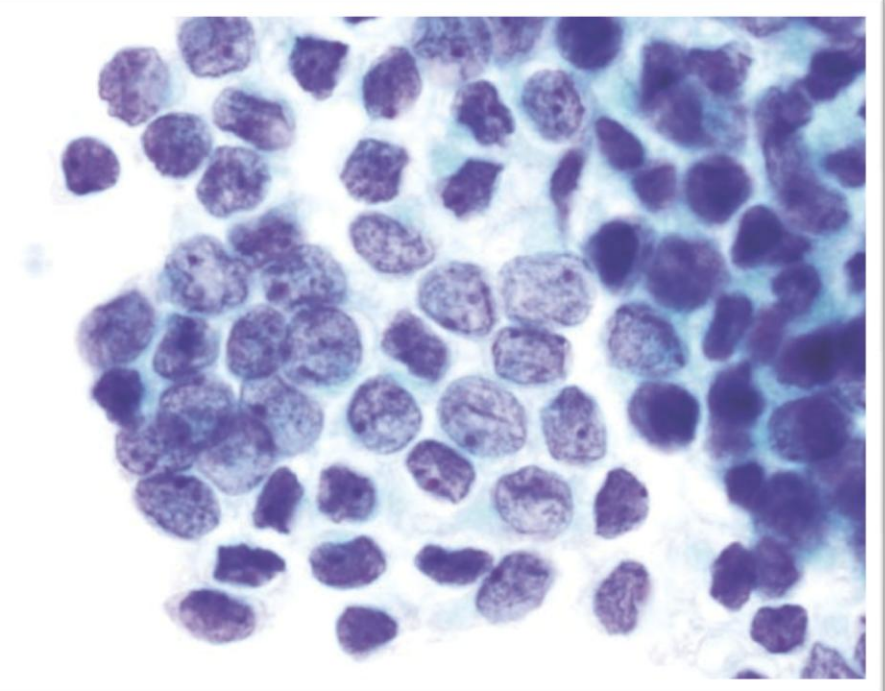
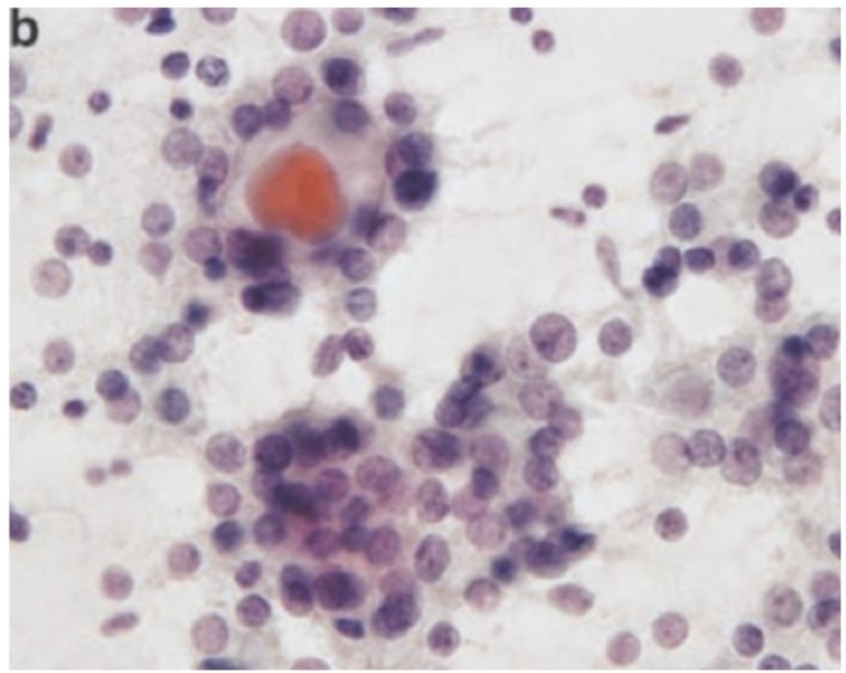
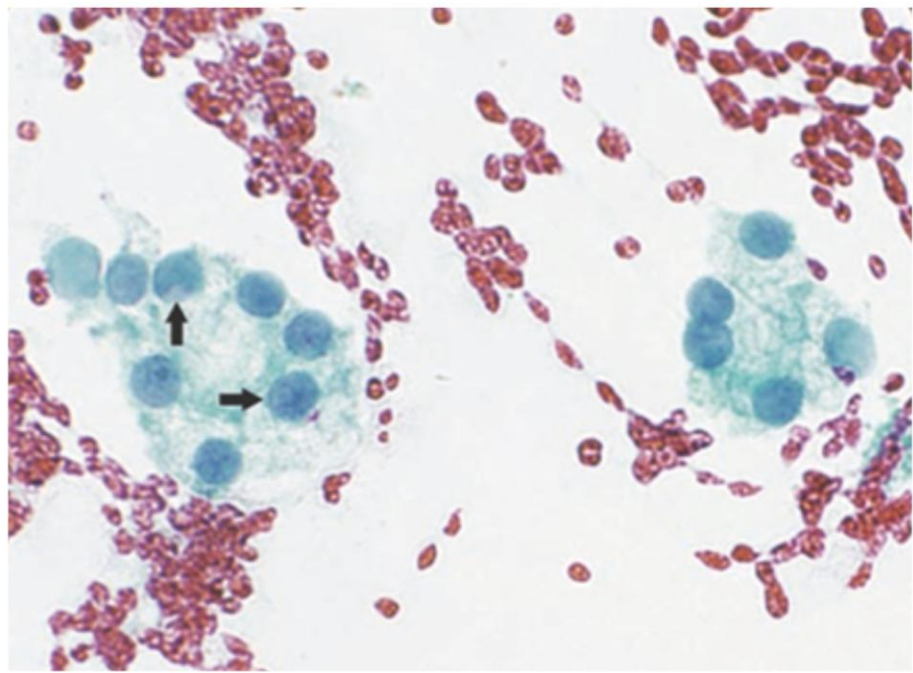
**Surgery Correlation Group**



**FIG. 2.** Correlation between cytology, molecular findings, and histological diagnosis in the surgery correlation group.

Mutasyon saptanan 32 nodülün 31'i malign

Herhangi bir mutasyon varlığı malignitenin güçlü bir göstergesidir.





**TABLE 1.1.** The Bethesda System for Reporting Thyroid Cytopathology; recommended diagnostic categories.

**I. Nondiagnostic or Unsatisfactory**

- Cyst fluid only
- Virtually acellular specimen
- Other (obscuring blood, clotting artifact, etc.)

**II. Benign**

- Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
- Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
- Consistent with granulomatous (subacute) thyroiditis
- Other

**III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance**

**IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm**

- specify if Hürthle cell (oncocytic) type

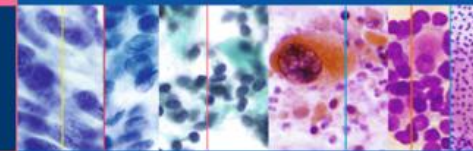
**V. Suspicious for Malignancy**

- Suspicious for papillary carcinoma
- Suspicious for medullary carcinoma
- Suspicious for metastatic carcinoma
- Suspicious for lymphoma
- Other

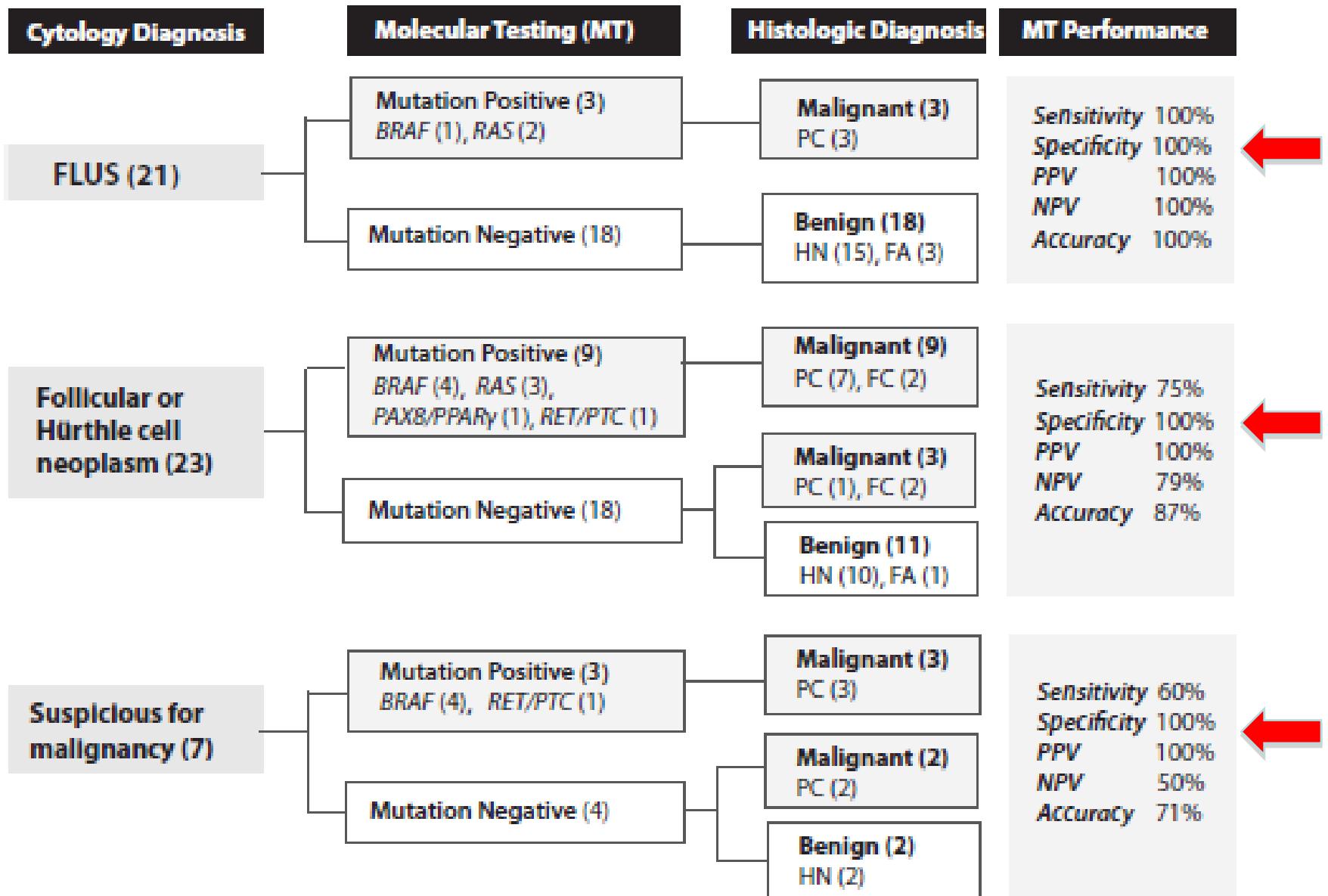
**VI. Malignant**

- Papillary thyroid carcinoma
- Poorly differentiated carcinoma
- Medullary thyroid carcinoma
- Undifferentiated (anaplastic) carcinoma
- Squamous cell carcinoma
- Carcinoma with mixed features (specify)
- Metastatic carcinoma
- Non-Hodgkin lymphoma
- Other

Syed Z. Ali • Edmund S. Cibas  
*Editors*



**The Bethesda  
System for  
Reporting Thyroid  
Cytopathology**  
Definitions, Criteria and  
Explanatory Notes





**TABLE 2.** Probability of cancer in thyroid nodules depending on the results of cytological and molecular analysis

| <b>Results of cytology and molecular analysis</b> | <b>Cancer probability (%)</b> |
|---|-------------------------------|
| Positive cytology and positive for mutation       | 100                           |
| Indeterminate cytology alone                      | 40.4                          |
| Indeterminate cytology and positive for mutation  | 100                           |
| Indeterminate cytology and negative for mutation  | 16.2                          |
| Negative cytology alone                           | 2.1                           |
| Negative cytology and negative for mutation       | 0.9                           |

# KEMİK İLİĞİ ASPİRASYON BİYOPSİSİ

- SINIFLAMA
- TANI
- TEDAVİ
- PROGNOZ

## **MYELOİD NEOPLAZİ TANISI**

Tam kan değerleri

Periferik yayma

Kemik iliği aspirasyonu

Kemik iliği biyopsisi

İmmunhistokimya-Akım sitometri

Sitogenetik

Moleküler incelemeler

## Prekürsör Lenfoid Neoplaziler

|   |        |
|---|--------|
| B lenfoblastik lösemi / lenfoma, daha ileri özelliği olmayan            | 9811/3 |
| B lenfoblastik lösemi / lenfoma, rekürren genetik anomalilerle birlikte |        |
| B lenfoblastik lösemi / lenfoma, t(9;22); bcr-abl1                      | 9812/3 |
| B lenfoblastik lösemi / lenfoma, t(v;11q23); MLL rearranged             | 9813/3 |
| B lenfoblastik lösemi / lenfoma, t(12;21); TEL-AML1 & ETV6-RUNX1        | 9814/3 |
| B lenfoblastik lösemi / lenfoma, hiperploidi ile                        | 9815/3 |
| B lenfoblastik lösemi / lenfoma, hipodiploidi ile                       | 9816/3 |
| B lenfoblastik lösemi / lenfoma, t(5;14); IL3-IGH                       | 9817/3 |
| B lenfoblastik lösemi / lenfoma, t(1;19); E2A-PBX1 & TCF3-PBX1          | 9818/3 |
| T lenfoblastik lösemi / lenfoma   | 9837/3 |

World Health Organization Classification of Tumours



Pathology & Genetics

Tumours of Haematopoietic and Lymphoid Tissues

Edited by Elaine S. Jaffe, Nancy Lee Harris, Harold Stein, James W. Vardiman



t(9;22) BCR-ABL1

JAK2 V617F

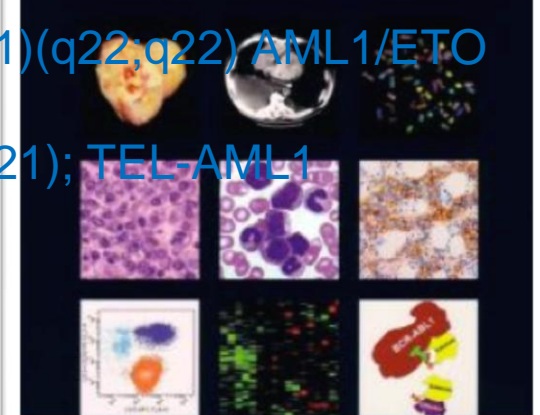
del(5q)

del(7q)

Inv(16)

WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

Edited by Steven H. Swerdlow, Elias Cernigoi, Nancy Lee Harris, Elaine S. Jaffe, Stefano A. Pileri, Harold Stein, Jürgen Thiele, James W. Vardiman



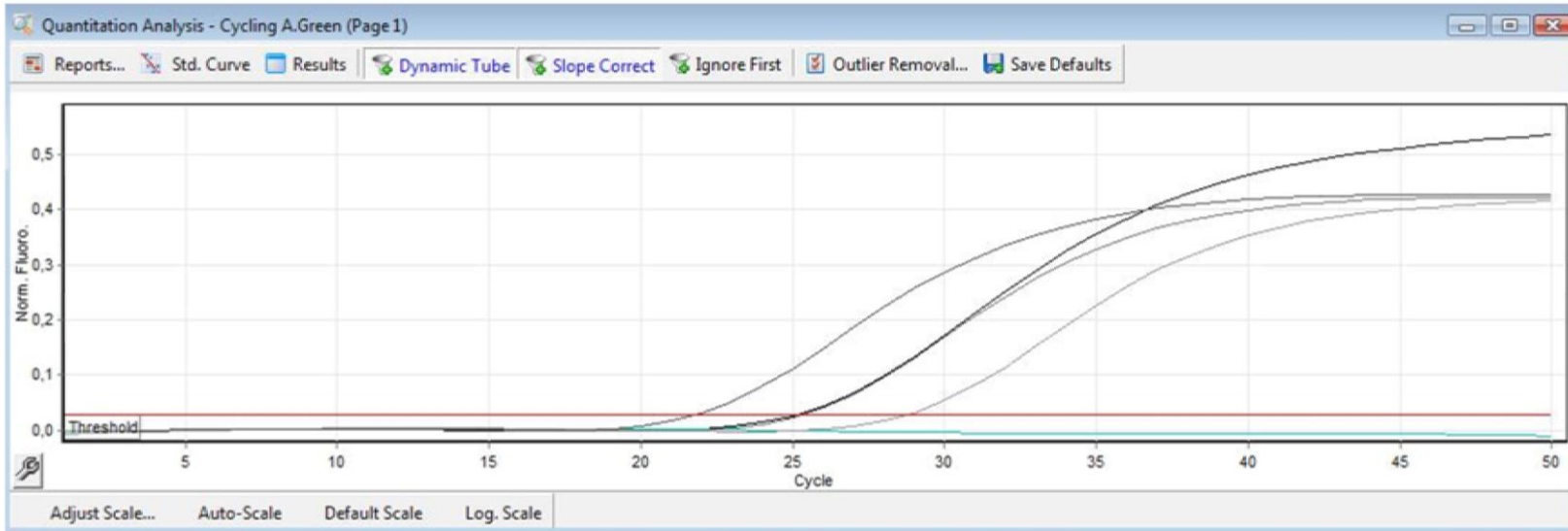
t(15;17)(q22;q12); PML-RARA

t(8;21)(q22;q22) AML1/ETO

t(12;21); TEL-AML1

# BCR-ABL

- 1960 Peter Nowell 'Philadelphia chromosome' tanımladı
- 1973 Janet D. Rowley translokasyon
- 1984 Groffen ve ark. Kromozom 9q34 üzerindeki ABL1 onkogenini ve kromozom 22q11 üzerindeki BCR "breakpoint cluster region" bölgesini tanımladılar
- 1985 Davis ve ark BCR-ABL hibrid geni normal ABL genine göre yüksek bir tirozin kinaz aktivitesine sahip olan bir kimerik protein sentezletir
- 1990 Daley ve ark bu protein KML patolojisindeki en önemli rolü üstlenir
- 3 izoformu
  - p190 genellikle akut lenfoblastik lösemi (ALL) ile
  - p210 genellikle kronik myeloid lösemi (KML) ile fakat ayrıca ALL ile
  - p230 genellikle kronik nötrofilik lösemi ile ilişkilidir



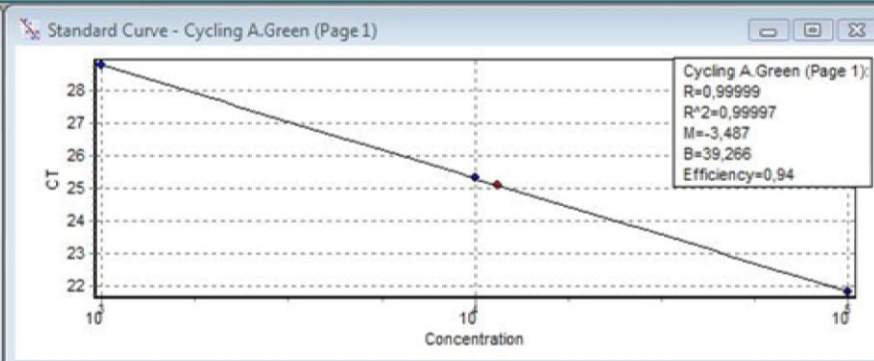
Page: Page 1

|    |         |
|----|---------|
| 17 | FG5     |
| 18 | 393 ABL |
| 19 | 397 ABL |
| 20 | 401 ABL |
| 21 | 403 ABL |
| 22 | 412 ABL |
| 23 | 416 ABL |
| 24 | 418 ABL |
| 25 | 421 ABL |
| 26 | 422 ABL |
| 27 | 433 ABL |
| 28 | 435 ABL |
| 29 | NTC ABL |
| 30 | ABL1    |
| 31 | ABL2    |
| 32 | ABL3    |

Bank On Bank Off  
Named On All On All Off  
Edit Samples...

Quant. Results - Cycling A.Green (Page 1)

| No. | Name   | Type     | Ct    | Given Conc (Cop) | Calc Conc (Copie) | % Var |
|-----|--------|----------|-------|------------------|-------------------|-------|
| 11  | 435 FG | Unknown  | 25,11 |                  | 11.488            |       |
| 12  | NTC-FG | Unknown  |       |                  |                   |       |
| 30  | ABL1   | Standard | 28,79 | 1.000            | 1.007             | 0,7%  |
| 31  | ABL2   | Standard | 25,34 | 10.000           | 9.863             | 1,4%  |
| 32  | ABL3   | Standard | 21,82 | 100.000          | 100.694           | 0,7%  |



CT Calculation

Invert Raw Data

Threshold: 0,02837

Eliminate Cycles before: 1

Auto-Find Threshold

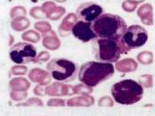
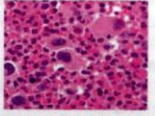
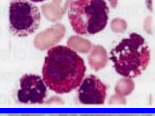
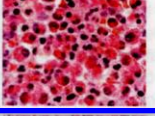
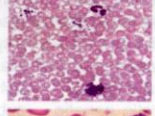
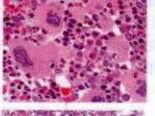
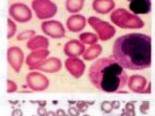
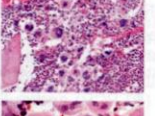
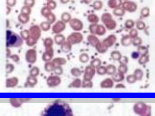
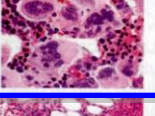
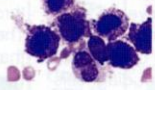
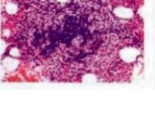
**Standard Curve**  
 $conc = 10^{[-0,287 \cdot CT + 11,260]}$   
 $CT = -3,487 \cdot \log(conc) + 39,266$   
 Type: Floating

Import Curve... Reset

Imported Settings >>

# JAK2

PV, ET, ve PMF için tanısal algoritmalar önemli ölçüde JAK2 V617F ve benzeri aktive mutasyonlar ile ilgili bilgileri içerecek şekilde değiştirilmiştir

|                                     |   |   |                                |
|-------------------------------------|---|---|--------------------------------|
| CML                                 |    |    | <i>ABL1</i>                    |
| Myeloid neoplasms with eosinophilia |    |    | <i>PDGFRA, PDGFRB, FGFR1</i>   |
| PV                                  |    |    | <i>JAK2 V617F, JAK exon 12</i> |
| PMF                                 |    |    | <i>JAK2 V617F, MPL W151L/K</i> |
| ET                                  |   |   | <i>JAK2 V617F, MPL W151L/K</i> |
| Mastocytosis                        |  |  | <i>KIT D816V</i>               |



# t(8;21), inv(16), t(15;17)

## Tekrarlayan genetik anomalilere sahip AML

t(8;21)(q22;q22); RUNX1-RUNX1T1 pozitif AML

inv(16)(p13.1q22) ya da t(16;16)(p13.1;q22);

CBFB-MYH11 pozitif AML

t(15;17)(q22;q12); PML-RARA pozitif akut promyelositik lösemi

t(9;11)(p22;q23); MLLT3-MLL pozitif AML

t(6;9)(p23;q34); DEK-NUP214 pozitif AML

inv(3)(q21q26.2) ya da t(3;21)(p21;q22); EVI1 pozitif AML

t(1;22)(p12;q13); RARA pozitif (akaryoblastik)

Mutant NPM1 pozitif AML

Mutant CEBPA pozitif AML

blast sayısı <%20

AML

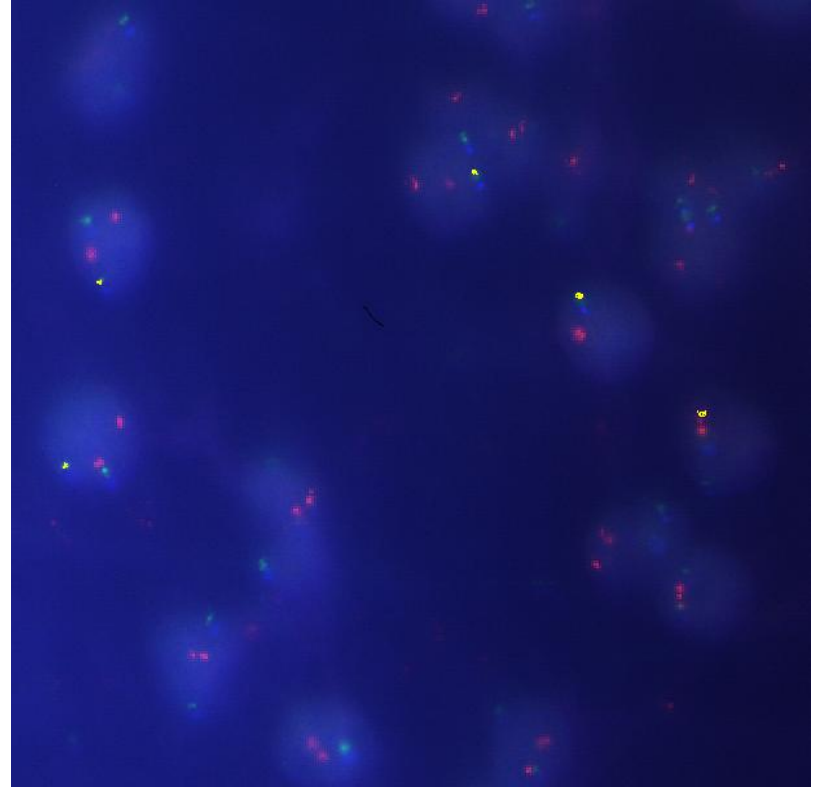
# del(5q)

- AML'de
  - t(8;21), inv (16), t(16;16), t(15;17) gibi sitogenetik bulgular tedavi yanıtının iyi olacağını göstergeleridir.
  - t(9;22), del(5q) kötü prognozu işaret eder.



# t(15;17)(q22;q12)

- Tedavi ile ilgili bir diđer örnek AML de t(15;17) nin gözleendiđi APL dir.
- Antrasiklinler ile kombine all-trans-retinoik asit (ATRA) tedavisi
  - Retinoik asit promiyelositlerin terminal diferansiyasyonunu sađlayarak olgun granüositlere dönüşümü ve hücrelerin yaşam döngüsünü tamamlayarak yok olmalarını sađlar
- Bu tedavi ve remisyon süresi FISH analizi ile kolaylıkla takip edilebilmektedir.



# t(12;21); TEL-AML1

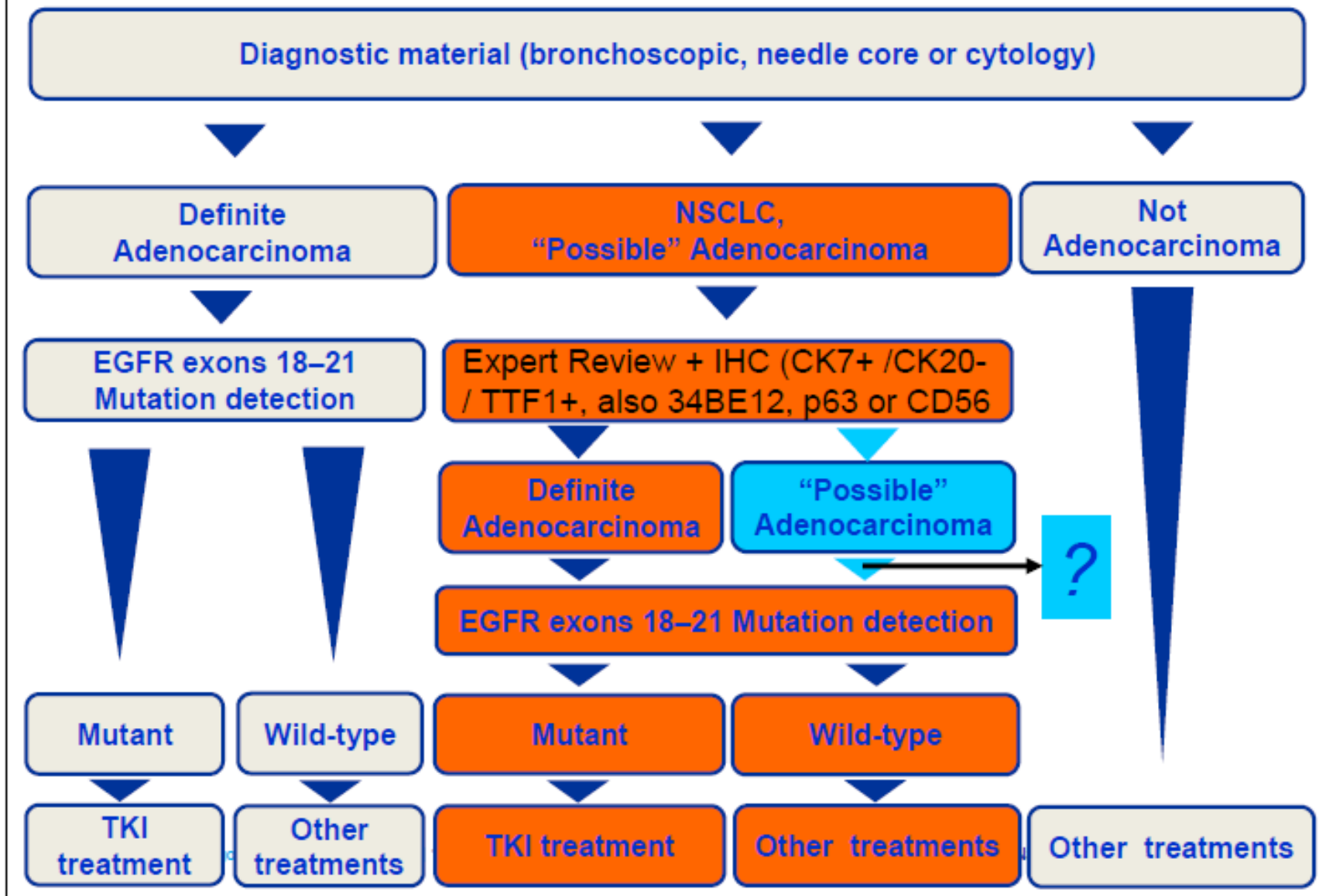
## Prekürsör Lenfoid Neoplaziler

|  |        |
|--|--------|
| B lenfoblastik lösemi / lenfoma, daha ileri özelliği olmayan                   | 9811/3 |
| <b>B lenfoblastik lösemi / lenfoma, rekürren genetik anomalilerle birlikte</b> |        |
| B lenfoblastik lösemi / lenfoma, t(9;22); bcr-abl1                             | 9812/3 |
| B lenfoblastik lösemi / lenfoma, t(v;11q23); MLL rearranged                    | 9813/3 |
| B lenfoblastik lösemi / lenfoma, t(12;21); TEL-AML1 & ETV6-RUNX1               | 9814/3 |
| B lenfoblastik lösemi / lenfoma, hiperploidi ile                               | 9815/3 |
| B lenfoblastik lösemi / lenfoma, hipodiploidi ile                              | 9816/3 |
| B lenfoblastik lösemi / lenfoma, t(5;14); IL3-IGH                              | 9817/3 |
| B lenfoblastik lösemi / lenfoma, t(1;19); E2A-PBX1 & TCF3-PBX1                 | 9818/3 |
| T lenfoblastik lösemi / lenfoma  | 9837/3 |

- B lenfoblastik lösemi/lenfoma spesifik kromozomal anormallikler içeren 7 farklı antiteye ayrılmıştır.
- Çocukluk çağı B ALL'lerinin %20-30'unu erişkinlerin %3'ünü oluşturur
- En sık görülen translokasyondur
- Kemoterapi yanıtından dolayı mükemmel prognoz. %100 remisyon

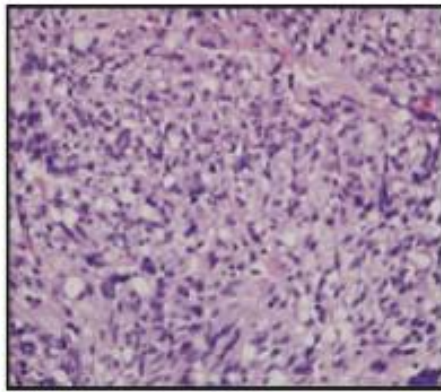
|                  |   |
|------------------|---|
| <b>SINIFLAMA</b> | WHO 2008'de Myeloid neoplazilerin ve akut lösemilerin majör subgruplarının her birine yeni antiteler eklenmiştir.   |
| <b>TANI</b>      | t(8;21), inv(16),t(16;16) veya t(15;17) varlığında blast sayısı <%20 olduğu zaman AML tanısı verilir  |
| <b>PROGNOZ</b>   | AML'de inv(16), t(8;21)(q22;q22), t(15;17)(q22;q12) <b>iyi prognoz</b><br>del 5q, del 7q, t(9;22) <b>kötü prognoz</b>   |
| <b>TEDAVİ</b>    | t(15;17) nin gözleendiği APL'de ATRA tedavisi   |
| <b>TAKİP</b>     | Minimal rezidüel hastalık: Başlangıç tedavisini takiben kronik miyeloid lösemi, akut promiyelositik lösemi ve çocukluk çağı akut lenfoblastik lösemilerinin faydalanma durumunun izlenmesinde |

# Pathology Sequence

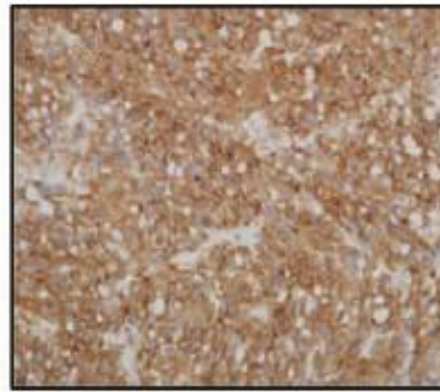




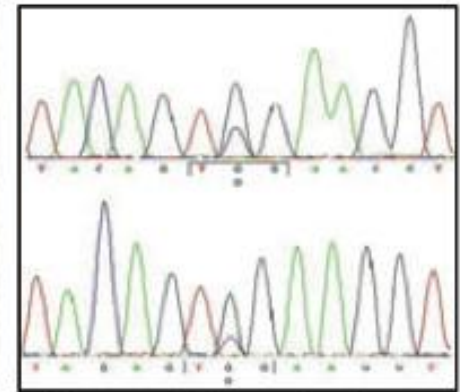
Partial gastrectomy: polypoid submucosal tumour of stomach



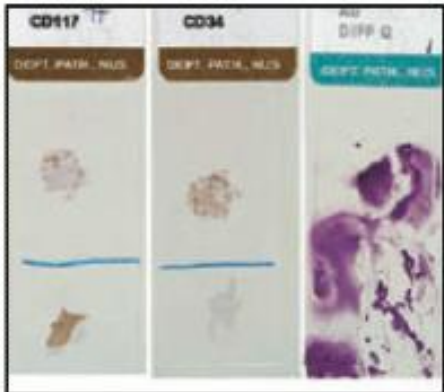
H & E section (x600): pre-dominantly spindled morphology



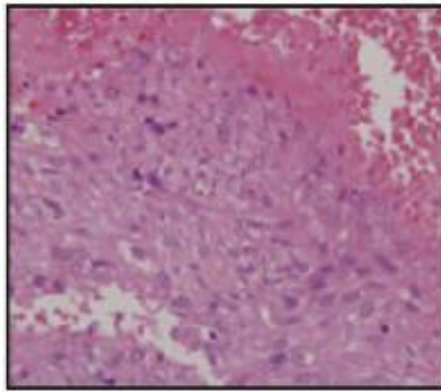
CD117 IHC on paraffin section: strong diffuse membrane positivity



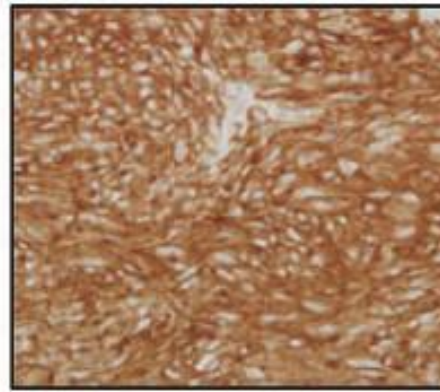
C-kit exon 11, forward and reverse sequencing: paraffin section



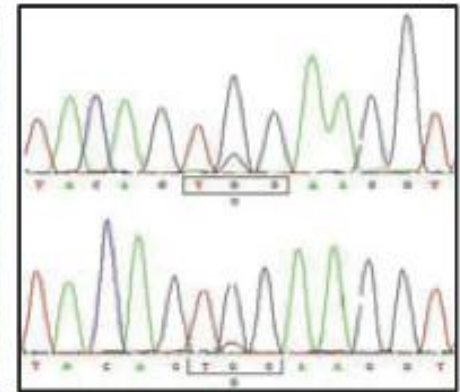
DQ smear preparation of pre-operative FNAC with cell block IHC for CD117 and CD34.



H & E section (x600) of cell block: pre-dominantly spindled morphology



CD117 IHC on cell block section: strong diffuse membrane positivity



C-kit exon 11, forward and reverse sequencing: cell block section

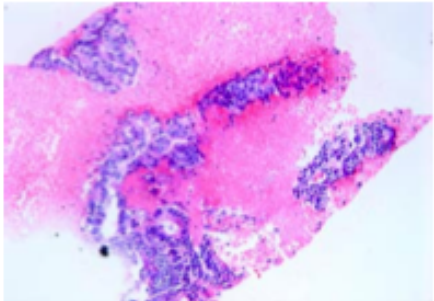
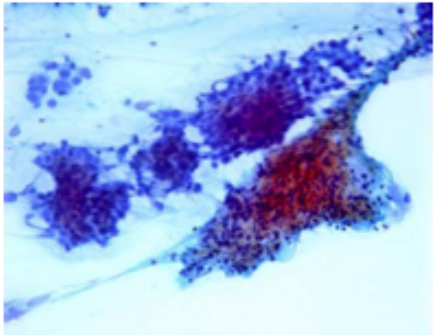
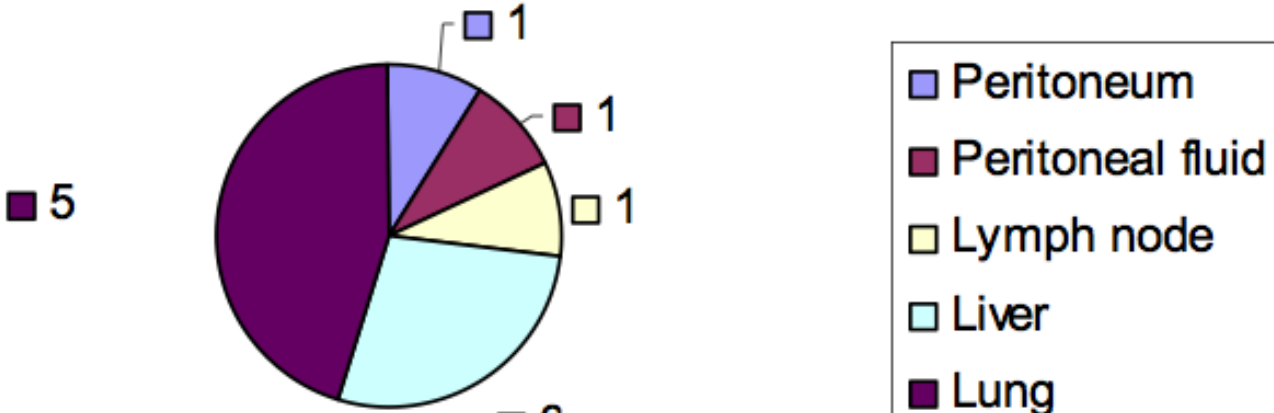
Pang NK, Chin SY, Nga ME, Chang AR, Ismail TM, Omar SS, Charlton A, Salto-Tellez M. Comparative validation of c-kit exon 11 mutation analysis on cytology samples and corresponding surgical resections of gastrointestinal stromal tumours. *Cytopathology* 2009;20(5):297-303



# KRAS and BRAF mutation analysis on cytology samples and corresponding surgical resections of colorectal carcinomas

**Pang NK, Chin SY, Nga ME, Ismail TM, & Salto-Tellez M.**

## Cytology samples analyzed for KRAS/BRAF mutations



Thus, only eight of the corresponding cytology cases were analysed. Seven of the eight cases tested showed the same KRAS genotype on both the aspirated cytology specimen of metastatic carcinoma and the primary tumour (histological specimen), from which we derive an overall concordance rate of 87.5%

# Avantajları

- Moleküler çalışmalar gerçekleştirmek için sitolojik materyalin doku kesitlerine pekçok avantajları vardır.
- DNA ve RNA sitoloji örneklerinde daha iyi korunur
- \*PCR için internal kontrol olarak beta-Globin kullanarak
  - Servikal sitoloji örneklerinin %100'ünde
  - Servikal biyopsilerin %66.7'sinde
- Sıvı bazlı koruyucu ortamlarda toplanan sitolojik örneklerden, formalinde fikse parafinize dokuya kıyasla daha kaliteli moleküler materyal elde edilir

\* Nonogaki S, Wakamatsu A, Longatto Filho A, et al Molecular strategies for identifying human papillomavirus infection in routinely processed samples: focus on paraffin sections. *J Low Genit Tract Dis.* 2005;9:219-224

# Sitolojik Tanı Örneklerinin Moleküler Analizinden Öğrendiklerimiz

- Jinekolojik, non-jinekolojik eksfoliyatif sitoloji yada İİAB örnekleri kullanılabilir
- PCR, RT-PCR, FISH, Pyrosekans, Sanger Sekans...
- Tanı, sınıflama, tedavi, prognoz hakkında bilgi verir
- Doku örneklerine kıyasla daha iyi sonuçlar elde edilebilir