PAPNext™

A Pap-Based DNA Test for Early Detection of Endometrial and Ovarian Cancers

eurofins | Genoma

Incidence and mortality of gynecological cancers

Despite the many recent advances in cancer diagnosis and treatment, gynecological cancers are responsible for approximately **25.000 deaths per year** and are the third leading cause of cancer-related mortality in women in the United States[1]. Most of the deaths are caused by tumors that metastasize prior to the onset of symptoms, in part because there are no accurate screening methods for these cancers and they are often diagnosed at a late stage.

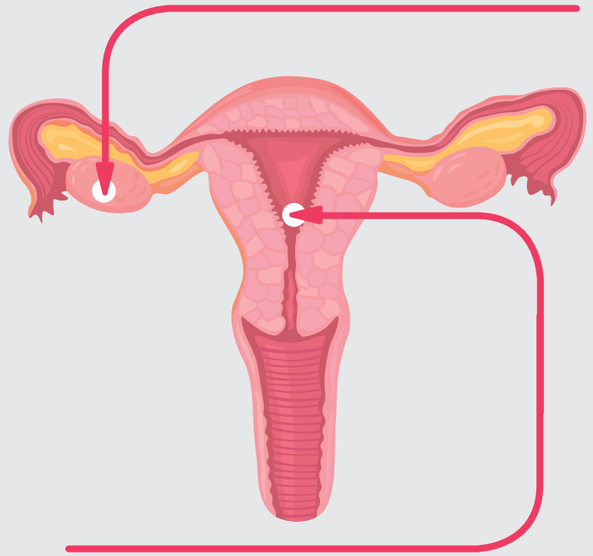
Worldwide, more than 200.000 deaths per year from gynecological cancers are expected[2,3].

The high mortality associated with undetected gynecologic malignancies has made the development of an effective screening tool a high priority.

Ovarian cancer is less common but more lethal.

It is often diagnosed at a late stage, when the 5-year survival rate is less than 30%.

- **More then 22.000 women in the U.S.[1]**
- **More then 14.000 deaths each year [1]**



Endometrial cancer is the most common gynecologic malignancy.

- **More then 62.000 new cases diagnosed in the U.S. each year [1]**
- **More then 11.000 women die each year from the disease[1]**

1) Howlader et al. SEER Cancer Statistics Review, 1975–2014 (National Cancer Institute, 2017).
2) Bray et al.. Int. J. Cancer 10.1002/ijc.27711 (2012).
3) International Agency for Research on Cancer, GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10; http://globocan.iarc.fr.

PAPNext™

Cervical fluid samples gathered during routine Pap tests are the basis of a revolutionary screening test for gynecological cancers

Prevention and early detection remain essential to decreasing cancer mortality. For many years, researchers have strived to develop a feasible and reliable way to detect early-stage gynecological cancers.

The introduction of routine screening for cervical cancer with cytology (the Papanicolaou test, otherwise known as **“Pap smear”**) has dramatically decreased the incidence and mortality of **cervical cancer** in the screened population, by permitting the detection of early-stage, surgically curable cervical tumors and their precursors.

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Unfortunately, the identification of malignant cells from **endometrial** and **ovarian** carcinomas in cervical cytology specimens is relatively uncommon. Microscopic examination cannot always distinguish them from cervical carcinomas, or from more benign conditions.

Screening DNA in Pap smears has the potential to increase the rate of early-stage detection of endometrial and ovarian cancers in women who do not have any symptoms. This DNA could be exploited to detect somatic mutations in tumor DNA released from endometrial and ovarian cancers shed cells accumulating in the cervix.

PAPNext™

A new dimension of screening for gynecologic cancers

Early detection of endometrial and ovarian cancers based on genetic analyses of DNA recovered from the fluids obtained during a routine Papanicolaou (Pap) test

PAPNext™ is a screening test that identifies cancer-related alterations in DNA obtained from cervical fluids gathered during a routine Pap test.

PAPNext™ test can detect endometrial and ovarian cancers at their **early stage**.
Earlier detection of cancer could lead to earlier treatment and potentially better outcomes for patients.

PAPNext™ test leverages the existing cervical screening strategy with an advanced sequencing technology to assess for DNA mutations in **30 genes** that are commonly mutated in endometrial, ovarian and cervical cancers, providing a cost-effective screening approach for these gynaecologic malignancies.

PAPNext™

Science behind the test

A recent study[4] demonstrated the ability to detect endometrial and ovarian cancer based on genetic analysis of DNA recovered from cervical fluids obtained during a routine Papanicolaou (Pap) test.

When an advanced sequencing technology was used to screen Pap test samples, gathered from women endometrial and ovarian cancers, for somatic mutations in DNA, the assay identified cancer-related alterations.

The assay identified cancer - related alteration in **93%*** of women with **endometrial cancer**

***90%**
(were early-stage cancers)

The assay identified cancer - related alteration in **45%**** of women with **ovarian cancer**

****47%**
(were early-stage cancers)

In addition, no cancer-related alterations were detected in samples collected from women without cancer, yielding a **very high specificity (>99.9%)**[5].

4) Kinde et alSci Transl Med. 2013 Jan 9;5(167):167ra45)
5) Wang et al. Sci Transl Med. 2018 Mar 21;10(433). pii: eaap8793.

Methodology

In-depth analysis of genes with advanced technology.

PAPNext™ test is performed using highly advances Next Generation Sequencing (NGS) technology to screen for tumor DNA mutation in **30 genes** that are commonly mutated in endometrial and ovarian cancers.

The technology is based on **full exon sequences**, at high sequence dept, of all genes included in the panel, which allow a more comprehensive analysis of each gene investigated.

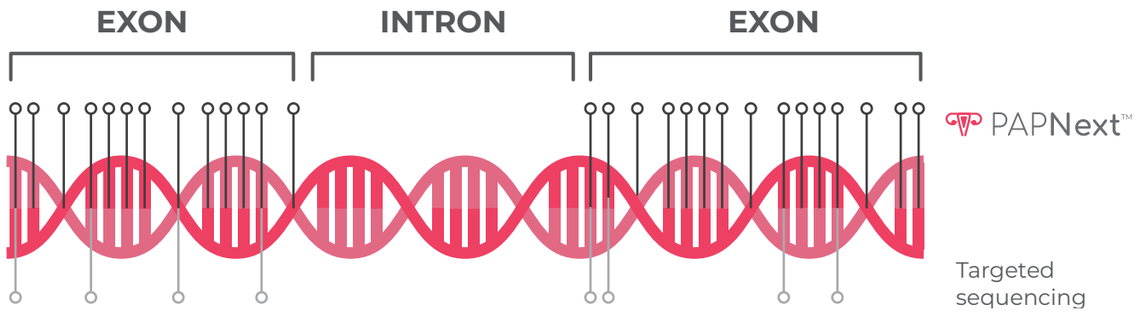
FULL-EXON SEQUENCING

PAPNext™ looks at the entire exom to identity all disease-causing mutations.

VS

Targeted sequencing

Focuses only on specific areas of the exon where mutations are associated with a disease



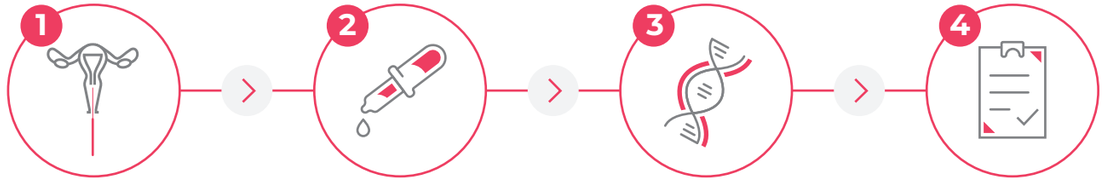
Bioinformatics

Advanced bioinformatic analysis for variant interpretation to deliver the greater accuracy.

Analysis of NGS data is a complex process, imposing challenging requirements both in terms of computing resources and software. PAPNext™ uses powerful custom-built bioinformatics solutions to support variant analysis that enables fast, reliable and highly accurate results.
When a variant is detected during the sequencing process, its pathogenicity will be investigated using a sophisticated software. A team of board-certified geneticists provide expert interpretation and clearly explained reports.

How PAPNext™ works

A Groundbreaking technology allowing for a genetic analysis that is revolutionary



Tumor DNA mutation screening in the targeted genes using an advanced bioinformatic analysis. The result are provided with a comprehensive technical report.

Understanding PAPNext™ results

POSITIVE RESULT

This result shows that the test **identified clinically relevant somatic mutation(s)** in tumor DNA, in one or more of the targeted genes screened.

A patient with a **positive test** result should be referred for genetic counselling before any medical decisions are made.

Genetic Cunselling

Genetic counselling is essential for any patient. Genoma will provide a genetic counselling session for those patients that screen positive, and the service is included in the cost of the test.
It aids the patients in medical comprehension and enhances patient satisfaction by providing access to experts who are skilled at explaining genetics risk in terms patients can understand.

NEGATIVE RESULT

This result shows the test **has not detected any clinical relevant mutation** in the targeted genes screened.

A single test cannot always detect all possible genetic changes that cause a particolar cancer condition, hence a negative results do not completely rule out the presence of malignancies screened.

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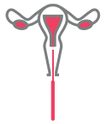
Benefits



PAPNext™ can be easily implemented as routine gynecological screening performed at the same time women undergo a Pap test for cervical cancer. The additional DNA analysis provided with PAPNext™ test is noninvasive and easily administered in the context of an annual gynecologic examination.

PAPNext™ testing has the potential to improve the conventional cytology screening for cervical cancer through the unambiguous detection of DNA from endometrial, ovarian and cervical carcinomas.

Most of the deaths are caused by tumors that metastatize prior to the onset of symptoms. PAPNext™ test allows early detection of endometrial, ovarian and cervical cancers at either a precancerous or early cancerous stage, when the disease is most curable.

Indications for testing

PAPNext™ test is meant for preventative surveillance of high-risk populations. It may be beneficial for (but not limited to):

Genetic predisposition

Patients with inherited predisposition to ovarian cancer, such as those with germline mutations in BRCA1 or BRCA2 gene or those with Lynch syndrome, caused by a germline mutation in MSH2 or MLH1 genes.

Risk factors

Patients who are at high risk for gynecologic cancers, e.g. because of hereditary factors, obesity, or symptoms such as postmenopausal or dysfunctional uterine bleeding.

Family History

Patients with a significant family history of endometrial and ovarian cancer.

Positive screen

Patients with positive conventional cytology screening test results

Early detection

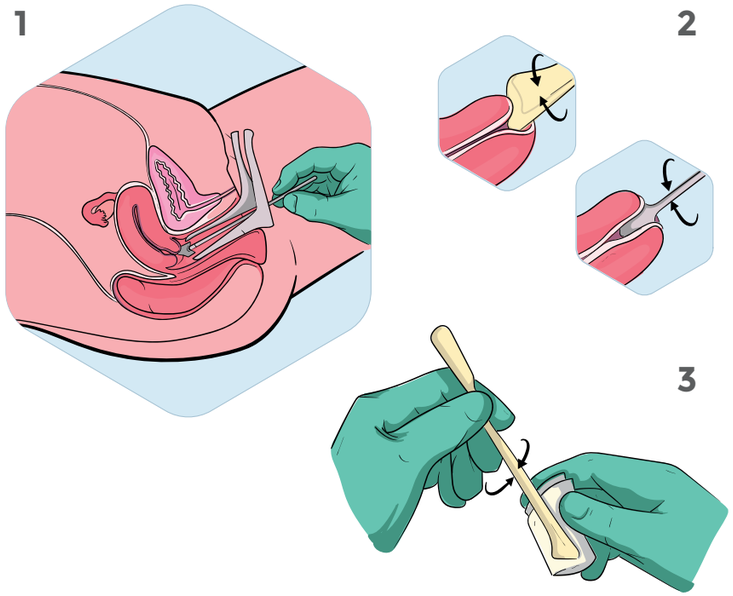
Any patient wishing to undergo to preventative surveillance for endometrial, ovarian and cervical cancers.

Sampling

Cancer cells are sampled during routine Pap tests with a brush (a "**Pap brush**") that is inserted into the endocervical canal to scrape the surface of the cervix and then rinsed in a liquid-filled vial containing preservative fluid.

For the detection of cervical cancers, cells from the fluid are applied to a slide for cytologic examination (the classic Pap smear). From the remaining sample, somatic mutations could be detected in tumor DNA of women with ovarian or endometrial, ovarian and cervical cancers.

Procedure



5 EASY STEPS

Order the PAPNext™ **shipping kit**

Fill in all requires **TRF** information and enclose the **informed consent signed** from the patient

Collect the sample (using the Pap brush provided with the shipping kit and rinse the brush in the liquid-filled vial)

Ship the sample to **Lab**

Receive results in as little as **10 days**

PAPNext™

Advanced molecular diagnostics solutions using state-of-the art technologies

Test performed in Italy
(Rome or MIlan)

Fast TAT: **15 days**

Overt than 20 years experience
in molecular diagnostics

Personalized genetic counseling
with genetic counselors experts in discussing genetic test results and familial risks

Laboratories **ISO 17025**
accredited with groundbreaking technologies

Test available
worldwide

Over **250.000** genetic tests/year

Dedicated R&D team
Numerous peer-reviewed papers published in renowned international journals

Design by evermind.it PapNext B Engl rev.01

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