Seegene Medical Foundation
ONE DAY test

Empowering global healthcare: Seegene Medical Foundation, your trusted partner in diagnostics

ONE TOPIC

HPV genotyping using real-time PCR

At Seegene Medical Foundation, our HPV Real-time PCR test is performed using the globally recognized Anyplex II HPV 28 product.

Press release (from MediPharm News)

Seegene cervical cancer test product receives top evaluation from WHO-affiliated agency

100% compliance with WHO recommendations in an evaluation of 119 global institutions ··· 'Perfect product'

Pharmaceutials/Bio

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Approved 2015.11.04 17:03:22

Seegene, Co. Ltd., (CEO Cheon, Jong-Yun, 096530) Cervical cancer testing product is recognized as the best product in the clinical evaluation conducted by HPV Laboratory Network, an affiliate of the World Health Organization (WHO).

The HPV Laboratory Network conducted a clinical evaluation of HPV diagnostic products, with participation from 119 institutions worldwide, including 68 in Europe, 14 in the Americas, and 8 in Southeast Asia. Seegene announced at the 30th International Papillomavirus Conference that its cancer diagnostic product outperformed global companies such as Roche and Abbott, receiving the highest evaluation.

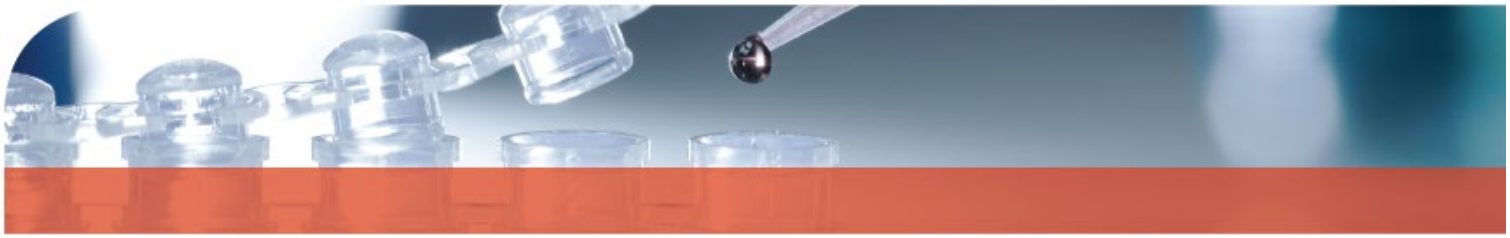
Since 2008, the HPV Laboratory Network has been conducting annual assessments to compare the accuracy and efficiency of HPV diagnostic products used by institutions worldwide. This year's assessment was the largest to date, with participation from 119 international testing institutions. The evaluation, based on WHO international standards, covered approximately 40 HPV diagnostic products around the world. The results revealed that Seegene's product demonstrated 100% compliance with WHO recommendations.

Cheon Jong-Yun, CEO of Seegene, stated, "Seegene's cervical cancer diagnostic product received the highest evaluation in a comparative assessment with numerous global companies. This reaffirms the excellence of our product. Particularly, the evaluation results from a reputable organization under WHO's jurisdiction are expected to have significant global impact."

Seegene's HPV diagnostic product can detect not only HPV types 16 and 18 but also up to 28 HPV genotypes, making it the most suitable product for cervical cancer diagnosis and monitoring. Unlike other cancers, cervical cancer has a clear cause (HPV), so early diagnosis is highly likely to lead to successful treatment. For this reason, WHO strongly recommends HPV DNA testing for the prevention of cervical cancer.

Seegene plans to lead the widespread adoption of cervical cancer DNA testing in Korea and internationally, leveraging its proven product performance recognized by a renowned global research institution.

Seegene Medical Foundation



Anyplex II HPV 28 is a globally recognized product, with 100% agreement rate in the comparative genotype assessment with 'WHO Reference Lab.

[Poster presentation : HPV 2015, 30th International Papillomavirus Conference, Sep. 17-21, 2015 Lisbon, Portugal]

"Continued global improvement in HPV DNA genotyping: The 2014 HPV LabNet International Proficiency Study"

Carina Eklund et al. (Karolinska Institute, Sweden)

Aim

HPV DNA genotyping methods used by institutions worldwide were evaluated through a blind test using standardized material to comparatively evaluate accuracy and performance.

Participation

- Participating institutions: 119 institutions (68 in Europe, 25 in Western pacific, 14 in the United States, 8 in Southeast Asia, 3 in Africa, 1 in Mediterranean)
- Test methods evaluated : 146 methods

Global HPV LabNet Genotyping Proficiency panel information

- Used International standard HPV DNA to ensure reproducibility
- Examine the ability to detect multiple infections
- Examine genotyping capacity
- Can be used in all HPV DNA assay methods
- HPV tested: 14 high-risk HPV types, 2 low-risk HPV types (HPV6,HPV11)
- Panel composition: plasmid DNA(42 ea), negative control(1 ea), extraction control(3 ea)

Requirements for Proficiency

- Sensitivity for HPV16, HPV18 detection: 50 IU / 5 uL
- Sensitivity for detection of other HPV types: 500 genome equivalent / 5 uL
- Must detect all HPVs in single and multiple infections
- Only one false positive permitted (97% specificity)

Seegene Anyplex™ II HPV28 Detection evaluation results
(See Table 1)

- 10 institutions worldwide participated, and all **"10 received 100% agreement."**
- **All HPV types detected in multiple infection samples with up to 5 types of HPV.**
- **Verified assay's** reproducibility, **sensitivity, and specificity**

Type of HPV assay	Number of datasets	100% proficient	99-90% proficient	89-80% proficient	<80% proficient	Not proficient
All assays	**146**	**86**	**16**	**9**	**5**	**30**
Linear Array (Roche)	14	7	1	1	0	5
HPV Direct Flow-chip (Master Diagnostica)	14	9	0	0	0	5
GenoFlow HPV array (DiagCor)	13	12	0	0	0	1
Anyplex™ II HPV 28 Detection (Seegene)	**10**	**10**	**0**	**0**	**0**	**0**
In- house PCR Luminex	8	3	1	1	0	3
In-house realtime PCR	8	4	0	1	1	2
In-house PGMY-CHUV	6	4	0	0	0	2
In-house blot	6	2	0	2	0	2
Papillocheck (Greiner)	5	4	0	1	0	0
Onclarity	**5**	**4**	**1**	**0**	**0**	**0**
CLART HPV 2 / 3 (Genomica)	4	0	1	1	2	0
Cobas 4800 (Roche)	**4**	**4**	**0**	**0**	**0**	**0**
InnoLiPA ()	4	1	2	0	0	1
PANA Realtyper 1001 (Panagene)	3	0	3	0	0	0
PANArray Genotyping Chip (Panagene)	**3**	**0**	**3**	**0**	**0**	**0**
Hybribio 21 HPV (Hybribio)	3	3	0	0	0	0
Realtime PCR (Abbott)	**3**	**1**	**0**	**2**	**0**	**0**
In-house sequencing	3	0	0	0	0	3
HPV SPF10-LiPA25	2	0	0	0	0	2
HPV XpressMatrix™ (DNA laboratories)	2	2	0	0	0	0
Ampliquality	2	0	1	0	0	1
Hybribio 13 HR (Hybribio)	2	2	0	0	0	0
Hybribio 14 HR (Hybribio)	2	2	0	0	0	0
PANA Realtyper 1002 (Panagene)	2	0	2	0	0	0
Optiplex (DIAMEX)	2	2	0	0	0	0
Other Commercial assays	14	9	1	0	1	3
Other In-house assays	2	1	0	0	1	0

[Table 1] 2014 HPV LabNet International Proficiency Evaluation Results

Anyplex II HPV 28 has been validated for its clinical performance in accordance with international guidelines for cervical cancer screening.

Equivalent sensitivity and specificity when compared with the reference

	clinical sensitivity	Clinical specificity
Target population	60 patients with ≥ CIN2	816 from general population with < CIN2
Reference	98.3% (59/60)	94.1% (768/816)
Seegene HPV product	98.3% (59/60)	93.6% (764/816)
Results	100%	99.5%
Standard	≥ 90%	≥ 98%

Comparison of Anyplex™ II HPV HR assay to Cobas 4800 HPV and Hybrid Capture 2 for the detection of high-risk HPV in PreservCyt specimens

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Introduction

Human papillomavirus (HPV) has been identified as the leading cause of cervical cancer in women[1]. The consolidated link between high-risk HPVs and cervical cancer has led to the introduction of HPV DNA testing in screening programs along with cytology testing[2]. The international validation guideline of novel HPV DNA tests for cervical cancer screening had been reported[3].

The Anyplex™ II HPV HR (Seegene Inc., Seoul, Korea) is a clinically validated multiplex real-time PCR assay for cervical cancer screening and is designed for the detection of 14 high-risk(hr) HPV with all individual genotypes information in a single tube. This is the first study to evaluate the clinical performances of Anyplex™II HPV HR Detection compared to those of FDA-approved assays with Korean women cervical specimens

Objective

The aim of this study is to evaluate clinical performances of Anyplex™II HPV HR Detection (Anyplex_HR) in comparison to those of Roche Cobas 4800 HPV test(Cobas_4800) and Hybrid Capture II (HC2).

Materials & Methods

- Anyplex_HR and HC2 were evaluated with 400 archived cervical samples (200 positive samples and 200 negative samples that tested by Cobas_4800).
- Cytology results of 400 samples were represented:

Cytological Level	ea
Negative for Intraepithelial Lesions or Malignancy (NILM)	290
Atypical Squamous Cells of Undetermined Significance (ASCUS)	40
Low-grade Squamous Intraepithelial Lesion (LSIL)	22
High-grade Squamous Intraepithelial Lesion (HSIL)	42
Atypical Glandular Cell (AGC)	6
Total	400

- All specimens were collected using Cobas PCR cell collection media. Anyplex_HR, Cobas_4800 and HC2 test were carried out according to manufacturers' instructions.
- The performance of Anyplex_HR for hrHPV genotype detection was retrospectively evaluated against HC2 and Cobas_4800.
- All discrepant samples were confirmed by PCR with PGMY09/11 and type-specific primers followed by sequencing.

References

1) Walboomers JM et al. *J Pathol* (1999) **189**:12-9
2) Ronco G et al. *Lancet* (2014) **383**:524-32
3) Meijer CJLM et al. *Int J Cancer* (2009) **124**(3):516-20

Results

- Concordance between Anyplex_HR and Cobas_4800 using clinical samples

			Cobas_4800			Agreement	*kappa*
			NEG	POS	Total		
Anyplex_HR	HPV16	NEG	354	2[a]	356	99.50%	0.975 (95% CI, 0.940-1.000)
		POS	0	44	44		
		Total	354	46	400		
	HPV18	NEG	388	0	388	99.75%	0.955 (95% CI, 0.868-1.000)
		POS	1[b]	11	12		
		Total	389	11	400		
	other HR	NEG	234	1[c]	235	98.75%	0.974 (95% CI, 0.952-0.997)
		POS	4[d]	161	165		
		Total	238	162	400		

- Overall agreement and kappa vales of Anyplex_HR with Cobas_4800 were 98.5% and 0.97, respectively. Agreement between two assays for HPV 16, HPV 18, and other hrHPV genotypes were 99.50%, 99.75%, and 98.75%. Most of discrepant results were obtained for positive samples with weak signal (Ct values ≥ 35).
- Confirmatory sequencing result of discrepancy samples
  a) Cobas_4800 true positive 1 ea, Anyplex_HR true negative 1 ea
  b) Anyplex_HR true positive
  c) Cobas_4800 true positive
  d) Anyplex_HR true positive 3 ea (HPV52 (2 ea), HPV68 (1 ea)), Cobas_4800 true negative 1 ea

- Overall concordance among three assay results (n=400)

		HC2			Agreement	*kappa*
		NEG	POS	Total		
Anyplex_HR	NEG	195	0	195	95.25%	0.905 (95% CI, 0.864-0.947)
	POS	19	186	205		
	Total	214	186	400		
Cobas_4800	NEG	198	2	200	95.50%	0.974 (95% CI, 0.869-0.951)
	POS	16	184	200		
	Total	214	186	400		

- Overall agreement and *kappa* value of Anyplex_HR and Cobas_4800 against to HC2 were over 95% and 0.9.

- Results of cervical cytology related to HPV DNA detection with Anyplex_HR and Cobas_4800

Assay	Positive rate (%) for samples with indicated cytology					
		Squamous cell abnormalities				Glandular cell abnormalities
	HPV genotypes	NILM (n=290)	ASCUS (n=40)	LSIL (n=22)	HSIL (n=42)	AGC (n=6)
HC2	Positivity	31.4	72.5	95.5	100	50
Anyplex_HR	Positivity	37.6	72.5	100	100	66.7
	HPV16	3.8	17.5	27.3	45.2	16.7
	HPV18	1.7	7.5	0	9.5	0
	Other HR types	32.8	57.5	81.8	64.3	50
Cobas_4800	Positivity	35.9	72.5	100	100	66.7
	HPV16	4.5	17.5	27.3	45.2	16.7
	HPV18	1.4	7.5	0	9.5	0
	Other HR types	31.7	57.5	81.8	64.3	50

- There was no difference in the detection rate of HPV between Anyplex_HR and Cobas_4800 in cytology results of ASCUS, LSIL and HSIL.
- From ASCUS stage, positivity rate and detection rate for each genotype of Anyplex_HR are equal to Cobas_4800.
- The sensitivities of both Anyplex_HR Detection and Cobas_4800 for LSIL/HSIL were 100%.

Conclusion

Anyplex™ II HPV HR Detection

1) is specifically designed for simultaneous detection of 14 high-risk HPVs including HPV16 and HPV18 with genotype information.
2) is comparable to Cobas 4800 HPV and HC2, it could be used for primary cervical screening.
3) would be useful for follow-up testing and patient management by providing genotype information beyond HPV16 and HPV18.

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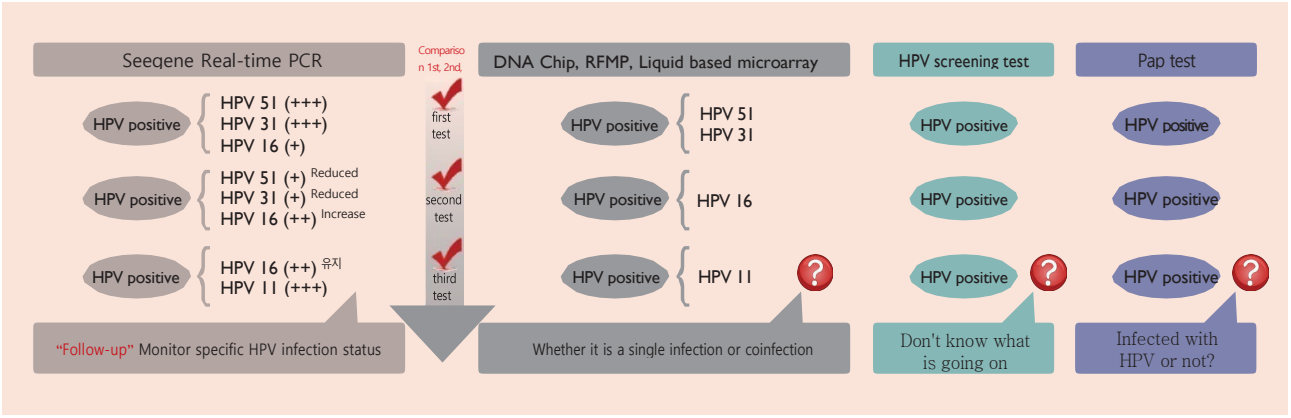
It is the most optimized assay enabling accurate follow-up of HPV infection

The benefits of HPV real-time PCR performed by Seegene Medical Foundation

For cervical cancer, it is important to check three points about HPV infection.
The first is to determine whether the infection is by a high-risk HPV, and second is to measure the viral load of the specific HPV genotype. The third is to determine the presence of multiple infections. In other words, the risk of cervical cancer increases with a more high-risk HPV, increasing viral load, and with multiple infections. Seegene Medical Foundation's HPV Real-time PCR is the only test that can identify the genotype, viral load, and multiple infection status required for follow-up of HPV infections. Also, it uses quality and performance-validated reagents approved by the MFDS [Approval 12-1699] and new health technology assessment that is also used in many university hospitals in Korea and abroad.

※ Using reagents that have not been approved by the Ministry of Food and Drug Safety (MFDS) for insurance coverage can lead to issues such as reduction or withdrawal of reimbursement.



You will have your results in a day (next morning after sample collection).

Collect sample on the day

Report results in 24 hours

Prompt patient treatment and prescription

The fastest molecular diagnostic test results reporting system

One-day test

What is a One-day test?

Seegene Medical Foundation has established the first automated molecular diagnostic testing system in Korea, which allows for a complete sample collection and reporting within 24 hours.

Types of One-day test

Seegene Medical Foundation realized the first system in Korea that provides one-day test results for the highest number of molecular diagnostic tests.

- HPV genotyping, multiplex Real-time PCR
- Genitourinary tract infection and sexually transmitted infections (STI) panel, PCR
- Respiratory Pathogen virus Panel, Multiplex real-time PCR (including Novel influenza A (H1N1))
- Respiratory Pathogen bacteria Panel, Multiplex real-time PCR
- Gastrointestinal Pathogen virus Panel, Multiplex real-time PCR
- Gastrointestinal Pathogen bacteria Panel, Multiplex real-time PCR
- Meningitis pathogen bacteria Panel, Multiplex PCR
- Hepatitis B Virus (HBV) Quantification, real-time PCR
- Hepatitis C Virus (HCV) Quantification, real-time PCR
- Mumps virus RT-PCR
- Helicobacter pylori real-time PCR
- Clarithromycin-resistant mutation, PCR

Usefulness of One-day tests

Increased early diagnosis rate

Prompt treatment of disease and prescription

Shortening of hospital re-visits

Seegene Medical Foundation

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SG-PE1053 Rev.(0) 2023.06