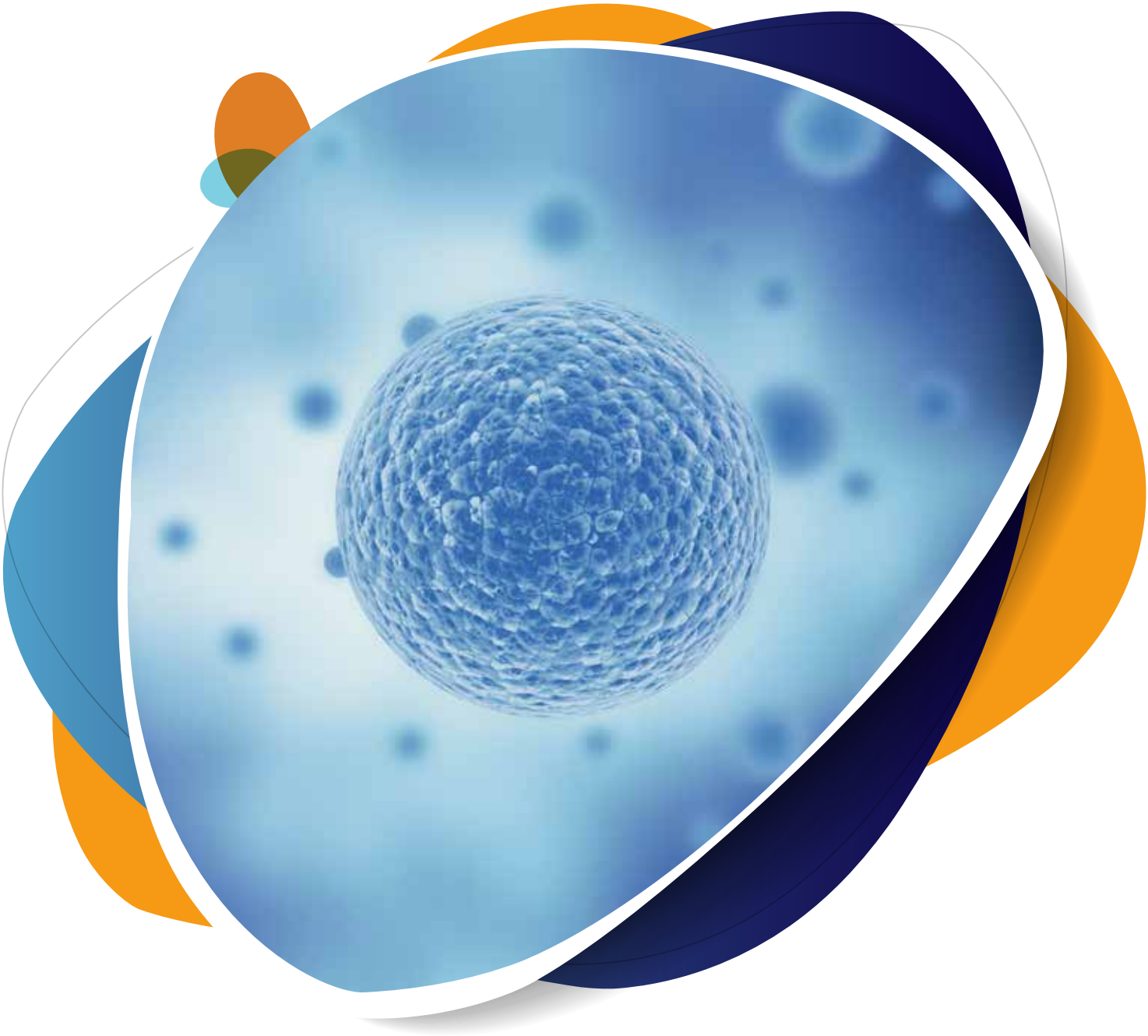
BPI

Benta incellDx®

HPV OncoTect® 3Dx



A Highly Specific Molecular Test for Early Detection of Cervical Cancer

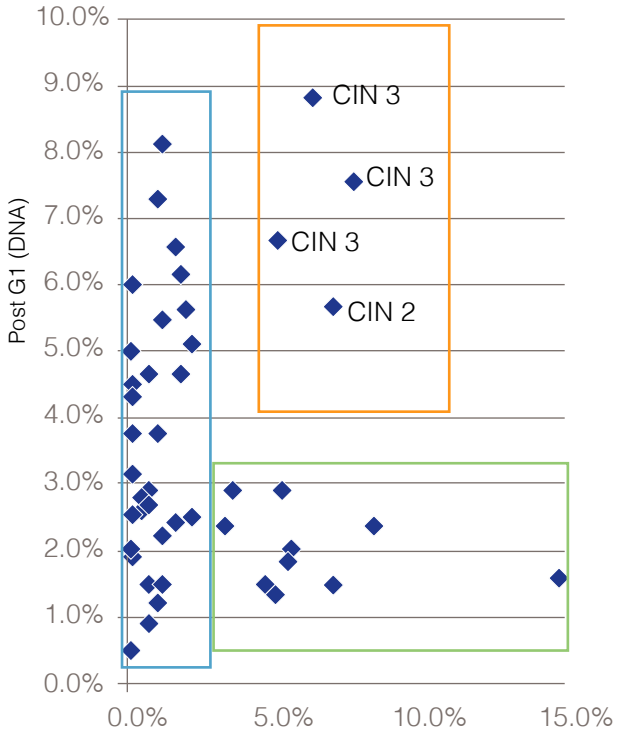
HPV E6,E7 mRNA + Cell Cycle

HPV OncoTect® 3Dx provides a unique single cell-based assay using flow cytometry

Unique to other methods, HPV OncoTect® 3Dx does not destroy the cell, allowing:

- ✓ Unambiguous identification of ectocervical cells [1,2,3,4]
- ✓ Quantification of E6,E7 mRNA overexpression[1,5], on two levels:
  - On a cell-by-cell basis [6]
  - Number of cells overexpressing E6/E7 in the squamous cell compartment of the cervical cytology specimen [6]
- ✓ Quantification of the percentage of cells in the proliferative stage of the cell cycle (Post G1)

High Grade
Low Grade
Normal cycling epithelium (ecocervical cells)



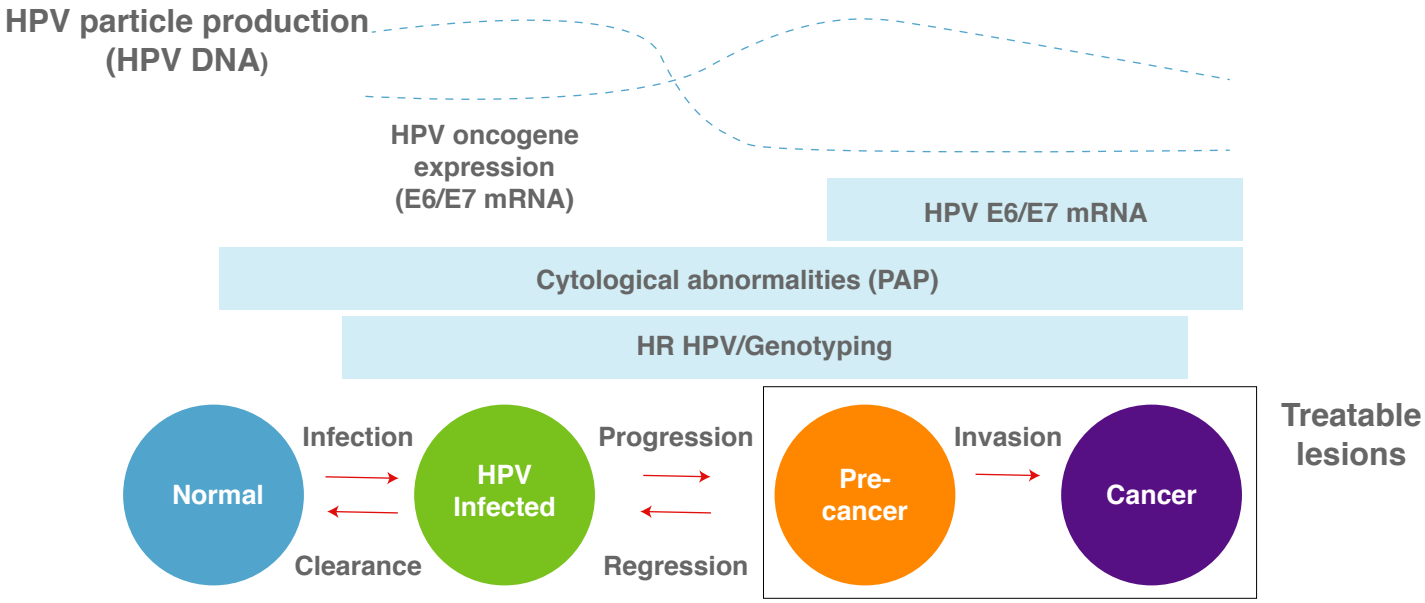
Proliferation and quantitative HPV mRNA distinguish high risk cases of HPV infection that are at higher risk of progression to cervical cancer [5, 7, 8, 9].

HPV OncoTect® 3Dx – CE-IVD

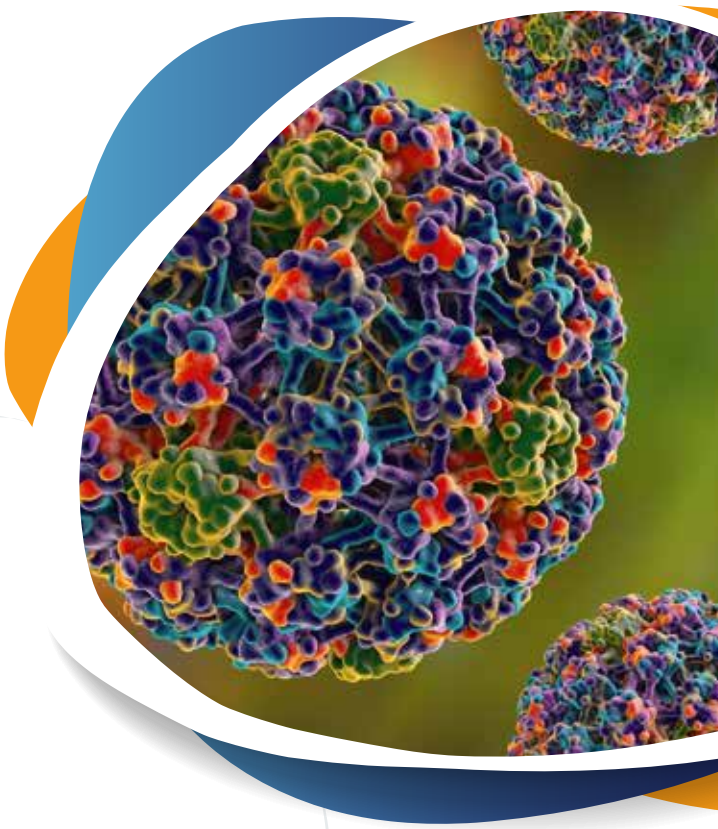
- For in vitro diagnostic use, CE-IVD, LDT
- Compatible with all commercial liquid-based cytology specimens
- 3-4 hour turnaround time
- Does not detect non-significant, transient HPV infections, delivering higher specificity and positive predictive values when compared to other HPV detection assays [5,6,10]
- Results potentially avoid unnecessary treatments, including unnecessary referrals to colposcopy [6,11], reducing overall costs

Cervical cancer is not HPV infection, but requires it

- ✓ Although the presence of HR HPV DNA is a necessary cause of cervical cancer [12], only a small percentage of HR HPV DNA infections result in pre-cancerous lesions (≥ CIN2) [13].
- ✓ E6 and E7 mRNA is considered to be a more specific indication of cellular transformation and the presence of ≥ CIN2 [3,10,14,15,16].

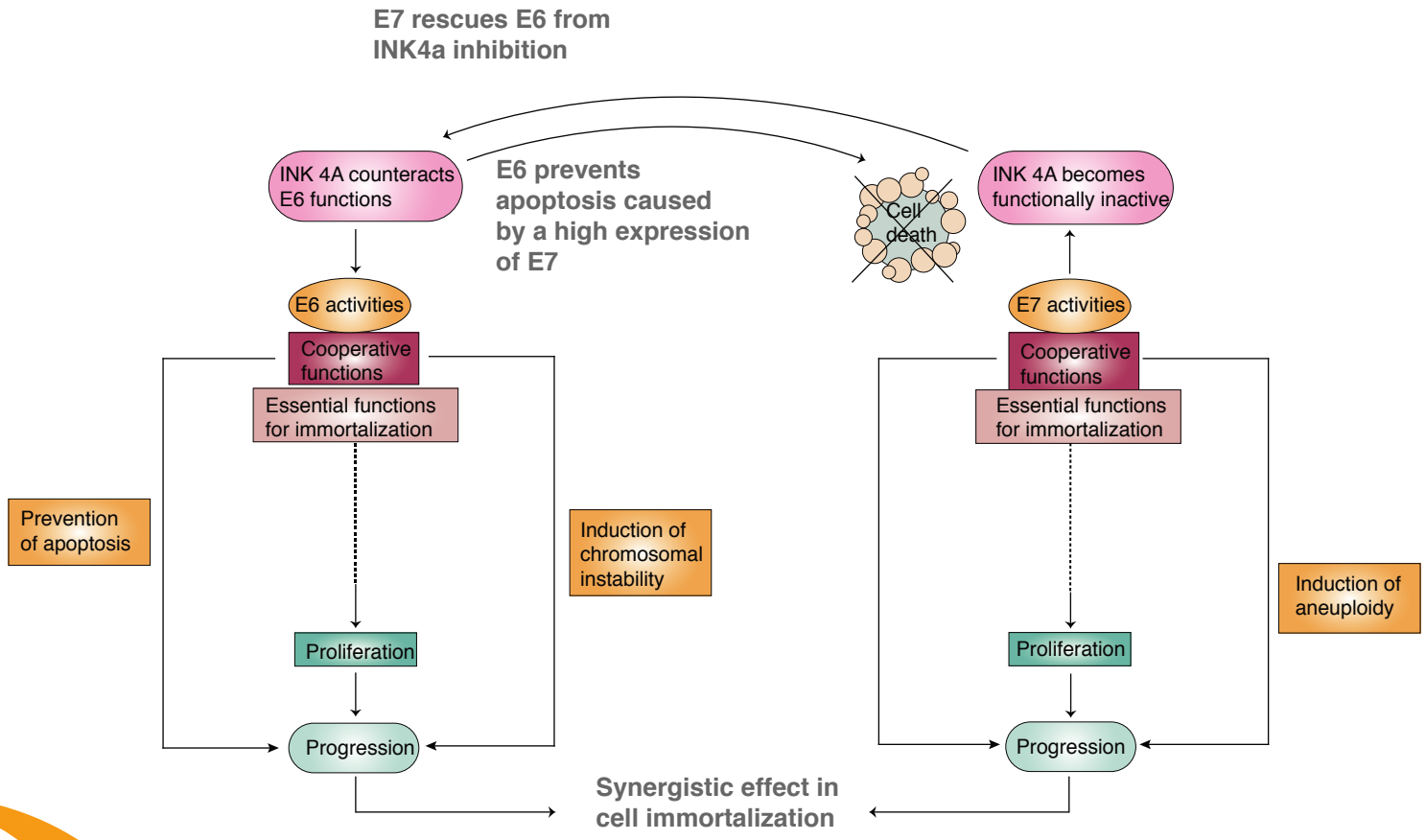


Cervical Cancer Biomarkers [17]



Overexpression of E6, E7 within the cell is what makes the difference

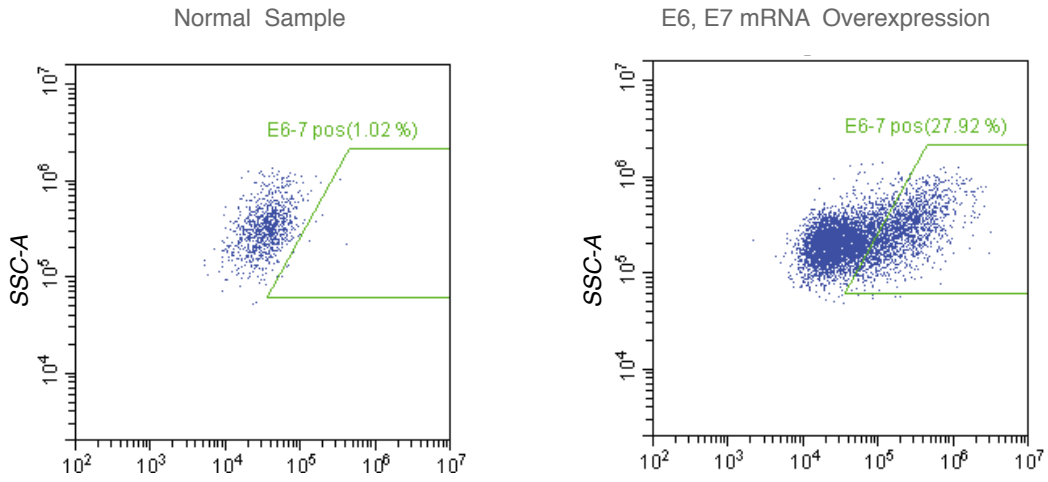
- ✓ In the life cycle of the HPV, the overexpression of E6, E7 mRNA in a cell is the molecular switch leading to cervical cancer[14,18,19,20].
- ✓ The HPV OncoTect® 3Dx Test is only positive if there is overexpression of E6,E7 mRNA and there is cell proliferation.



Mechanism of HPV-Induced Cervical Cancer [14]

By quantifying viral oncogenic activity, HPV OncoTect® 3Dx can differentiate between infection and CIN2+ lesions caused by HPV

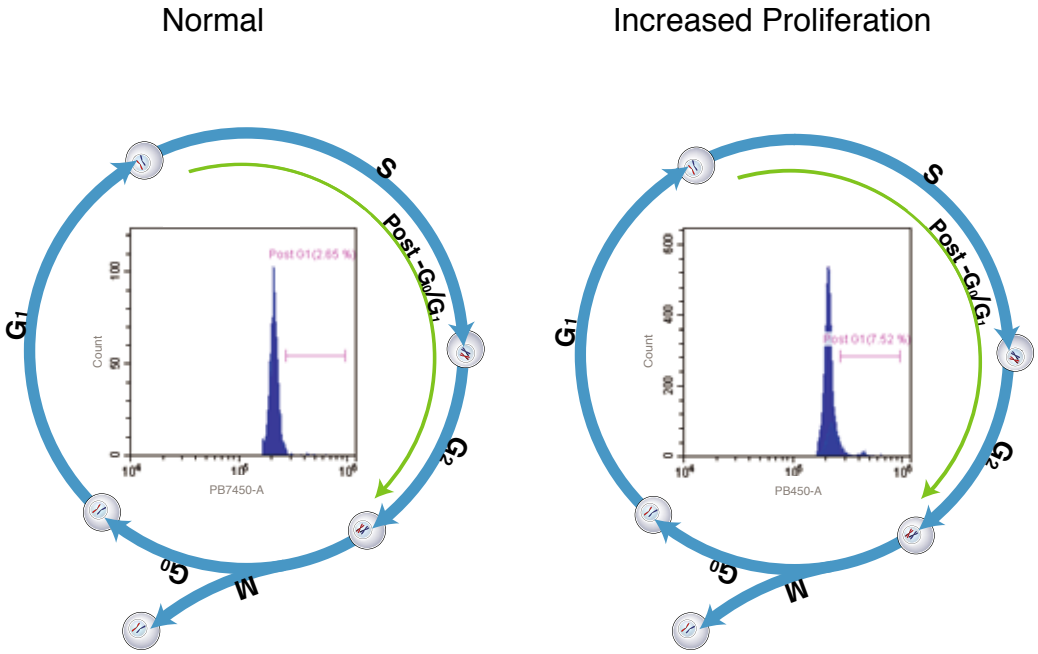
E6,E7 mRNA Overexpression



IncellDx HPV OncoTect® 3Dx E6, E7 mRNA, data on file

- Ectocervical cells are selected using forward and side scatter
- E6,E7 mRNA overexpression is objectively detected using the FITC channel

DNA Cell Cycle



NOTE: Cell Cycle Dye DNA stained, data on file

- Cell Cycle Dye staining reflects the cell cycle stage – resting (G0) to active replication (post G0/G1)
  - ◊ The secondary peak (x-axis) Indicates increasing DNA content and proliferation activity
- Compatible with most commercially available flow cytometers using forward and side scatter detectors with blue and violet lasers

HPV OncoTect® 3Dx delivers multiple parameters:

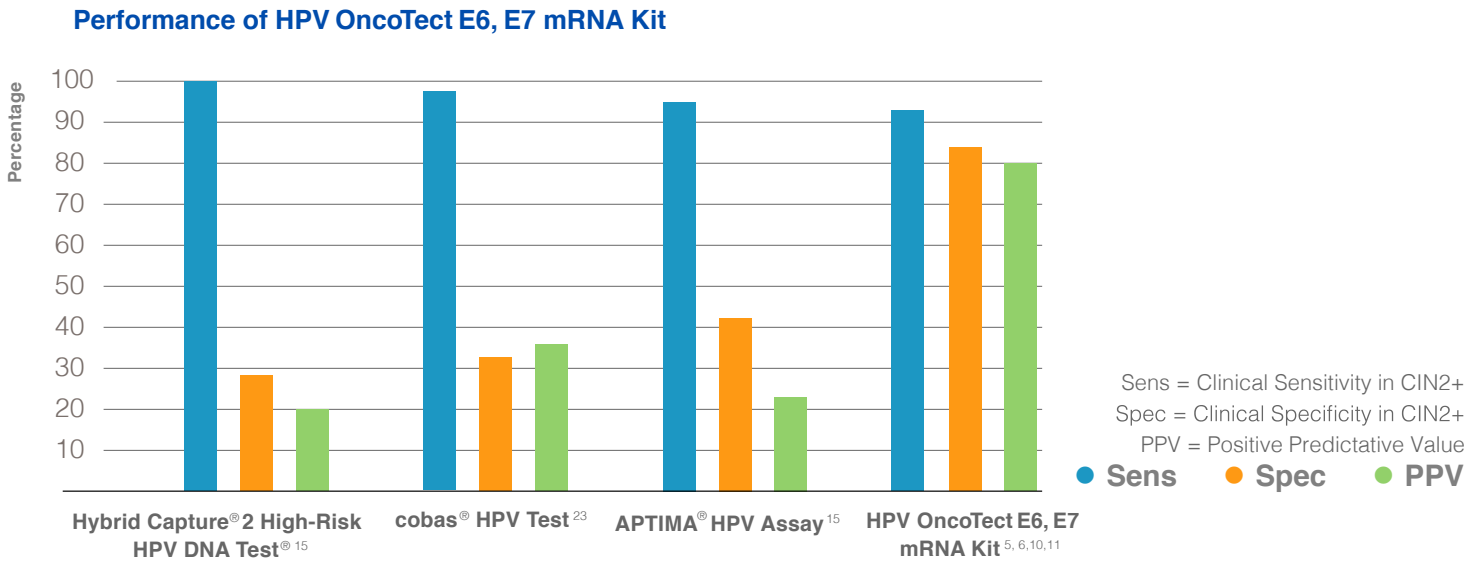
✓ Detection of E6, E7 mRNA overexpression, which is a specific indication of HPV DNA integration, DNA translation and cellular transformation [21]

✓ Detection of cells in the proliferative stage of the cell cycle (Post G1)

Product Design Features

Suggested Clinical Decision Point	≥ 4.6% of cells expressing E6,E7 mRNA and ≥ 4.0% of cells proliferating (Post G1%)
Specimens	Benta preservative solution
Result Interpretation	Positive or Negative, based on clinical decision cut-off

HPV OncoTect® 3Dx offers clinical sensitivity that is equivalent to high-risk HPV DNA tests [5,22] while increasing the specificity [5,12]



HPV OncoTect® is a registered trademark of IncellDx. Inc.

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