SMARTube™

Window Period Detection of HCV Antibodies by *in-vitro* Lymphocyte Stimulation

Presented at the CDC-HCV-2011 Symposium: Identification, Screening and Surveillance of HCV Infections in the Era of Improved Therapy for Hepatitis C

By: Tamar Jehuda-Cohen PhD

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Diagnosis of HCV - Challenges of antibody testing

1. **Long window period** – need tools for early detection

2. **High (and variable) levels of false positive**, the rate changing from population to population

   A major concern as it means:

   I. **Epidemiologically** - over estimating prevalence

   II. **Blood supply** - loss of good blood units.

3. **Routine antibody testing in serum does not differentiate between current / chronic infection and cleared / resolved infection**

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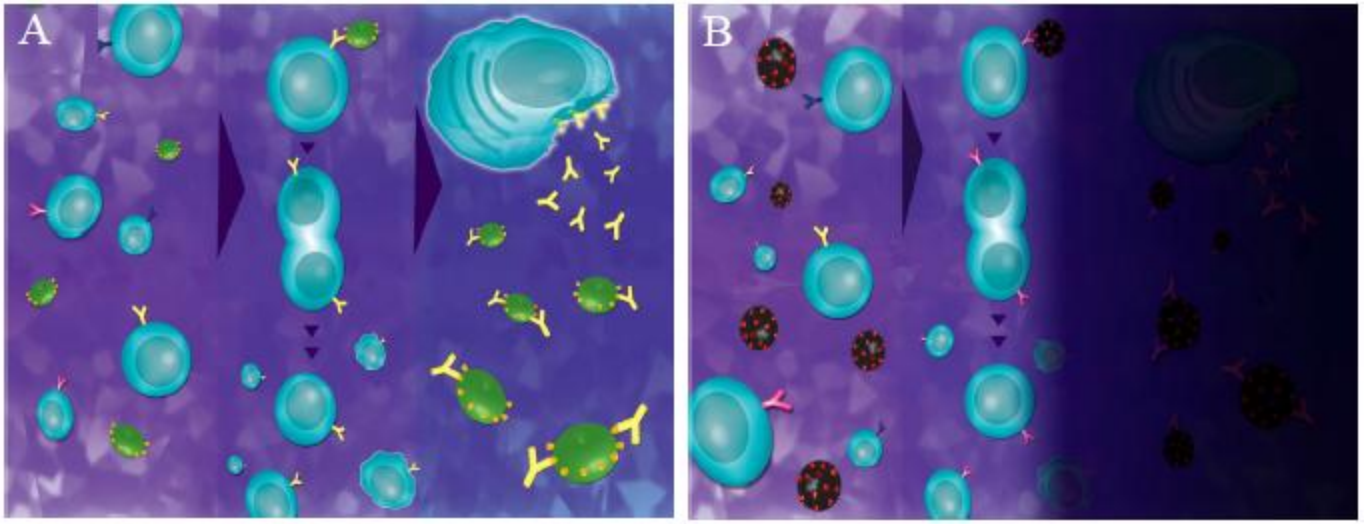
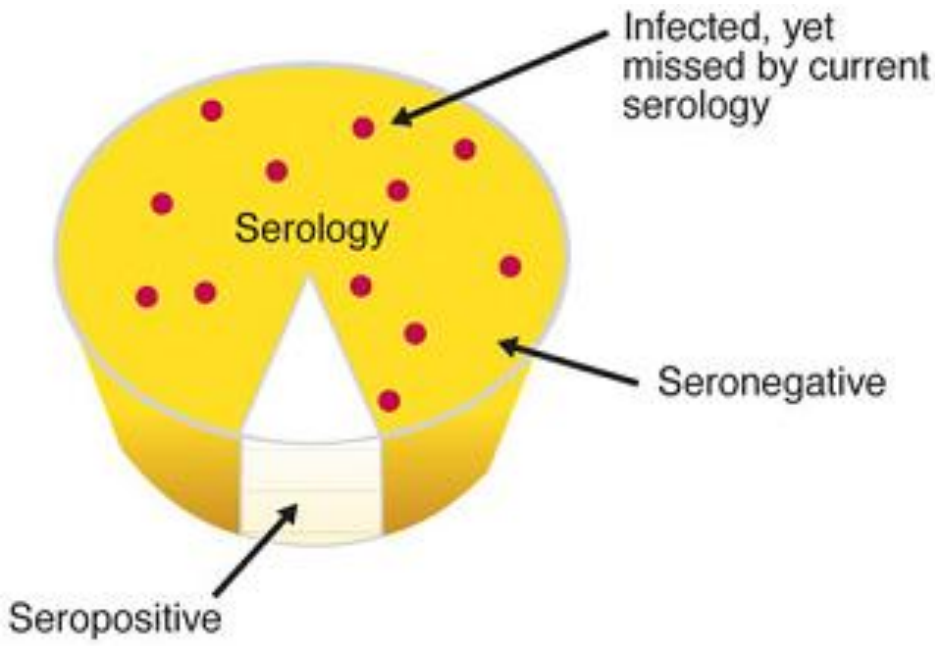
Diagnosis of HCV - Challenges of antibody testing

1. **Long window period** – need tools for early detection



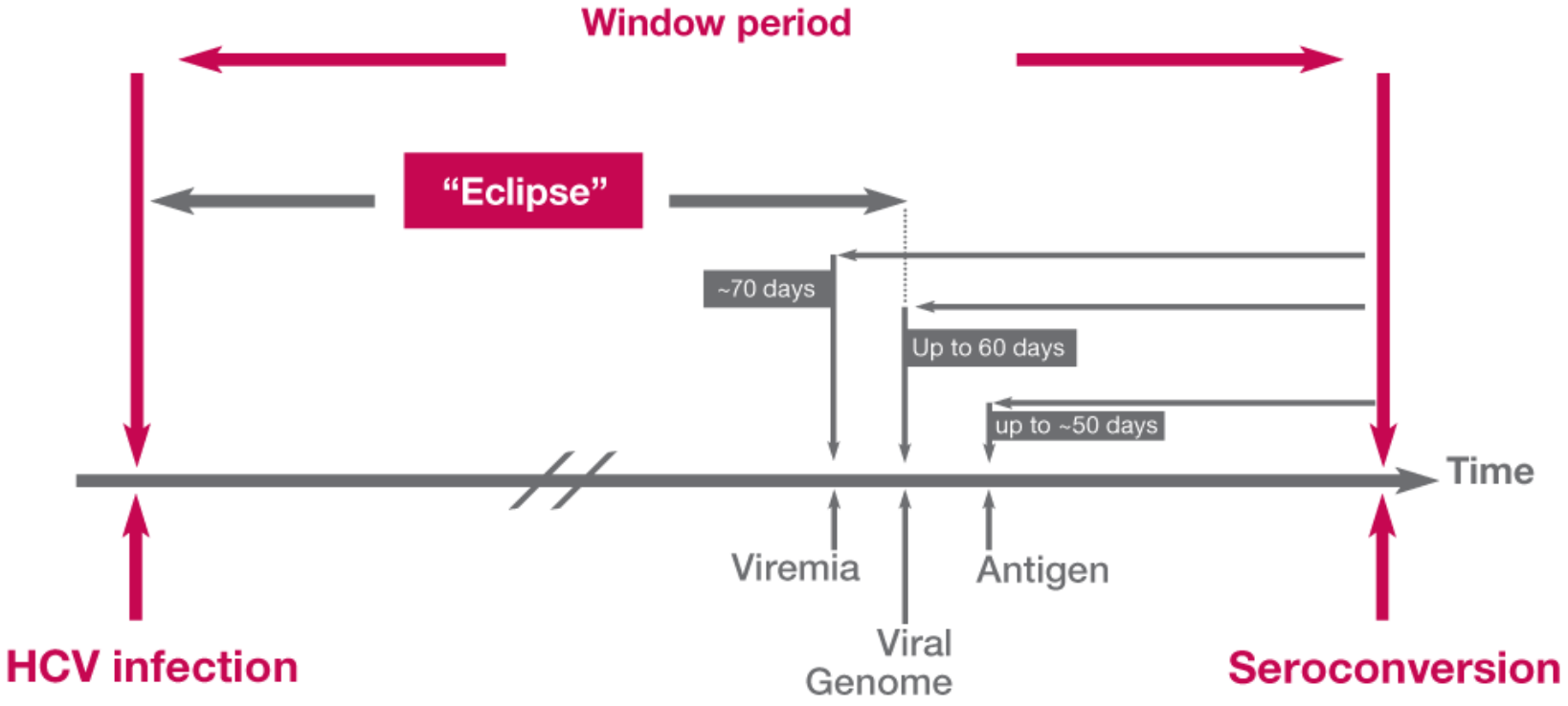
The HIV and HCV Problem:

Missed infections in the Window Period



- In a high risk group, seronegative results require repeat testing several months later.
- When the reason for liver damage is sought, a negative HCV result could lead to liver biopsies.
- In tracking / mapping a potential HCV outbreak, the most recent infections are missed.

The HCV Window Period: Shortening Methods



Stimmunology™

A Platform Technology:

Enhancement of antibody production (in-vitro) in a blood sample, even when facing immune suppression, enabling virus primed B-cells (which might have been 'silenced' in-vivo) to mature to plasma cells in-vitro.

Antibodies which were not present or detectable would be present in Stimmunology™ treated sample.

Both IgG and IgM antibodies are enhanced.

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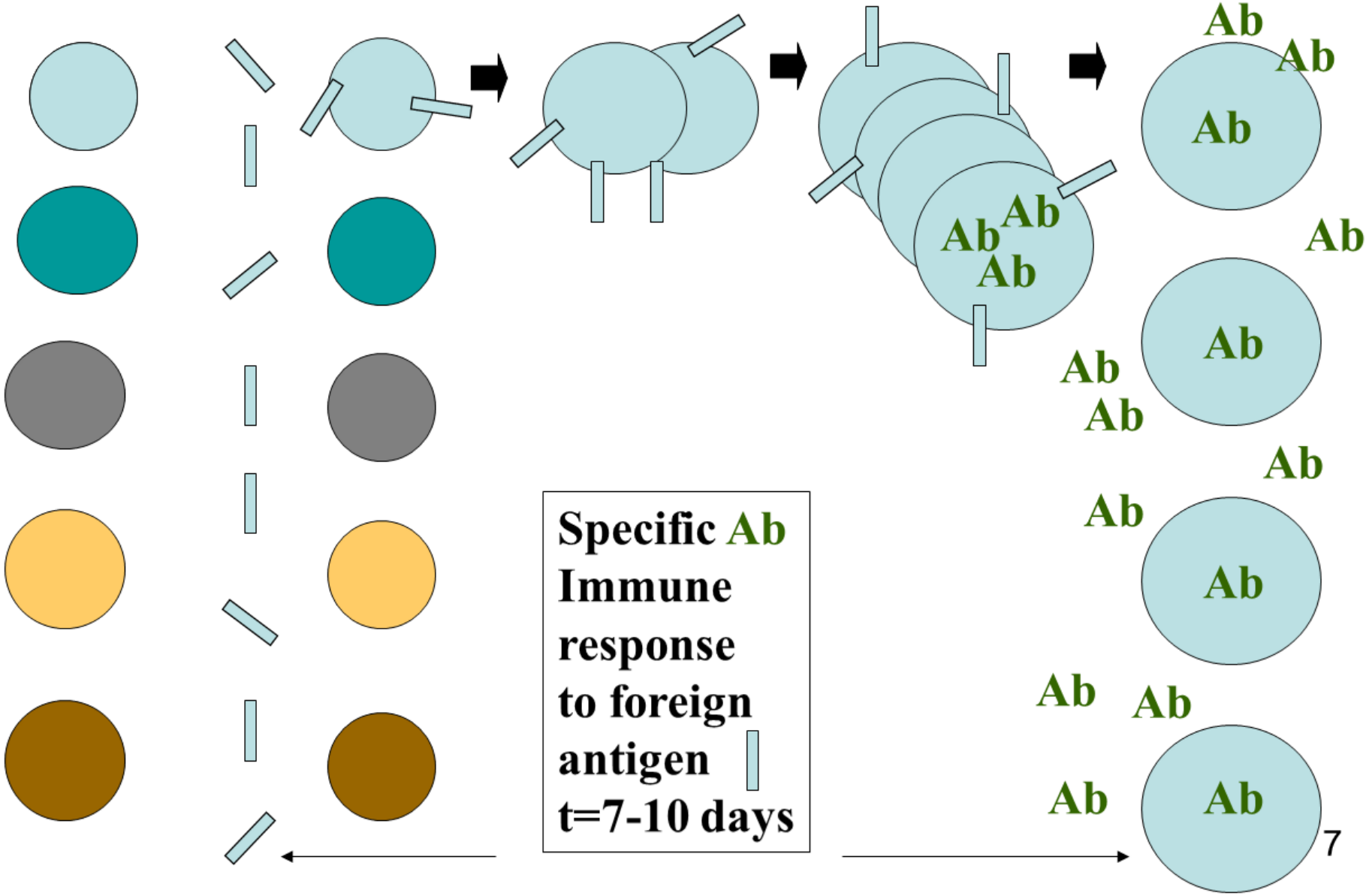
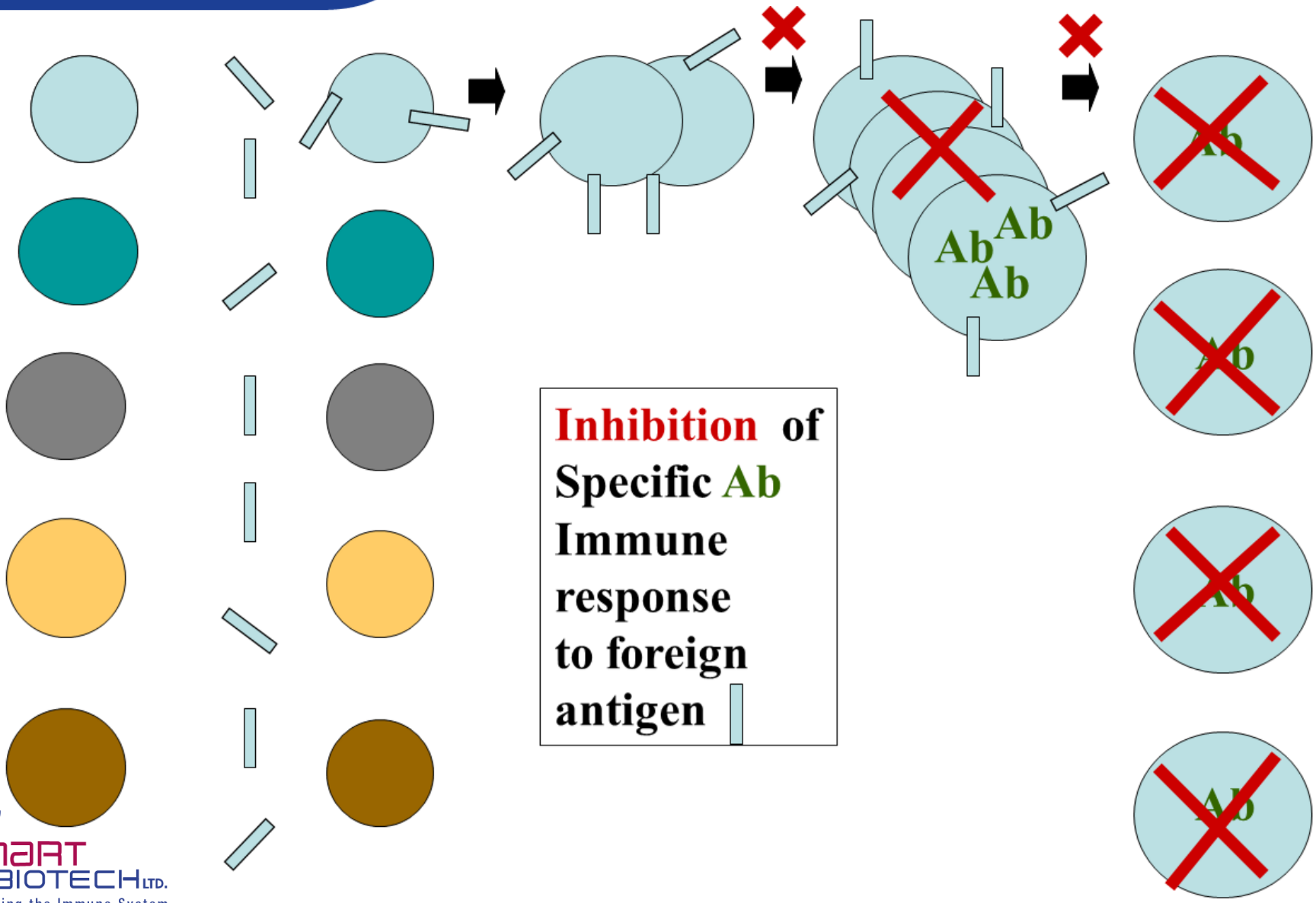
Stimmunology™



Stimmunology™



Inhibition of Specific Ab Immune response to foreign antigen

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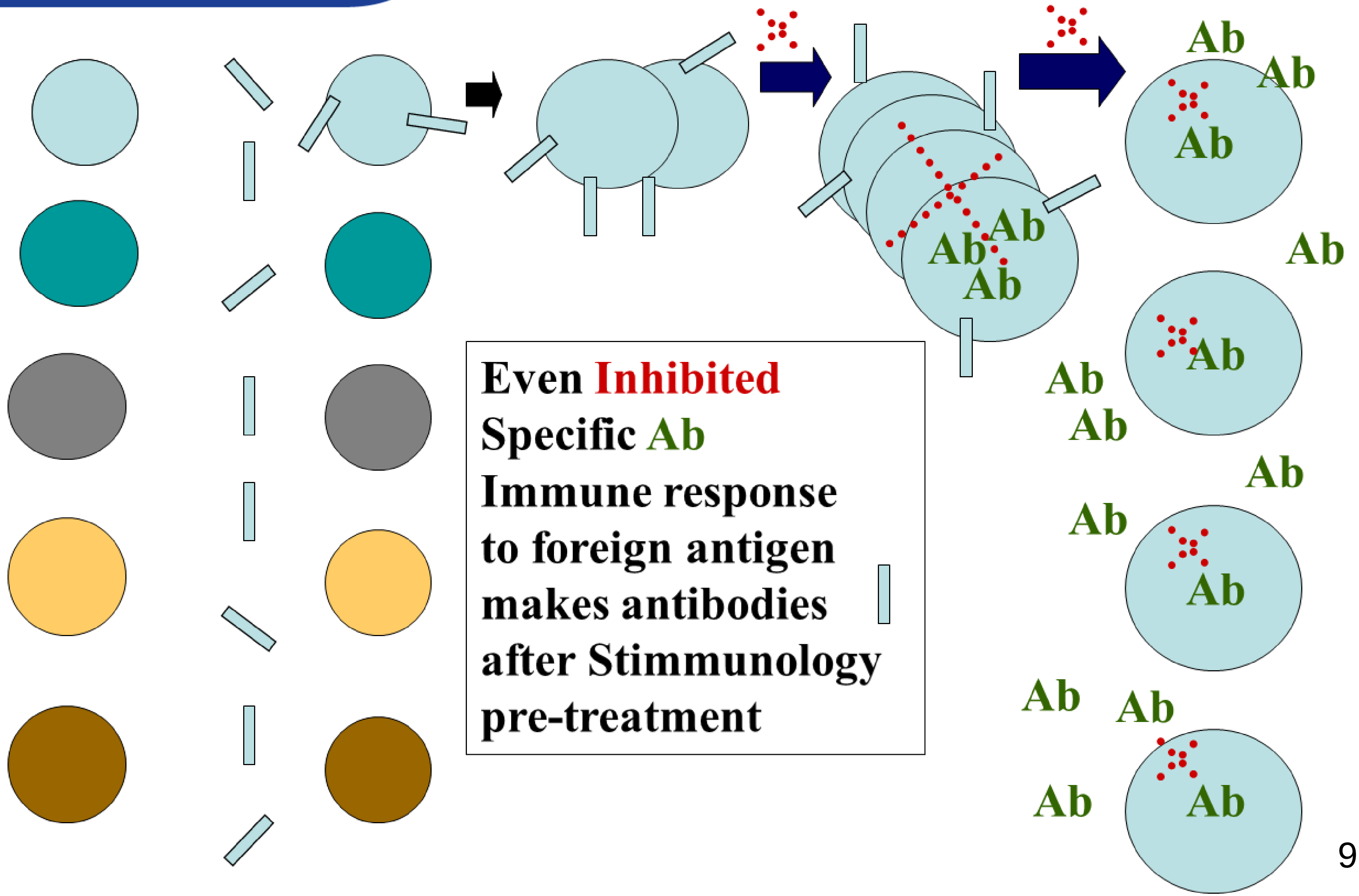
Stimmunology™



Even Inhibited
Specific Ab
Immune response
to foreign antigen
makes antibodies
after Stimmunology
pre-treatment

The solution: SMARTube™

S timulating
M aximal
A ntibody
R esponse
Tube

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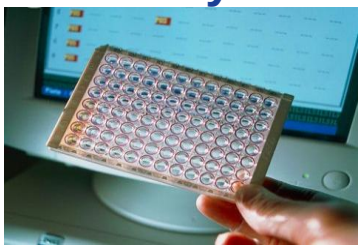
The Solution

- Family of products called **SMARTube™** based on the platform technology- Stimmunology™.
- **SMARTube™** - a pre-analytic device (treating the blood before testing) enabling detection of various infections within days of infection using currently available antibody tests (e.g. EIA, Rapid test, Blots, etc').

Draw blood

Transfer 1 ml into the SMARTube and incubate

Antibody test



ELISA
RIBA
Rapid test

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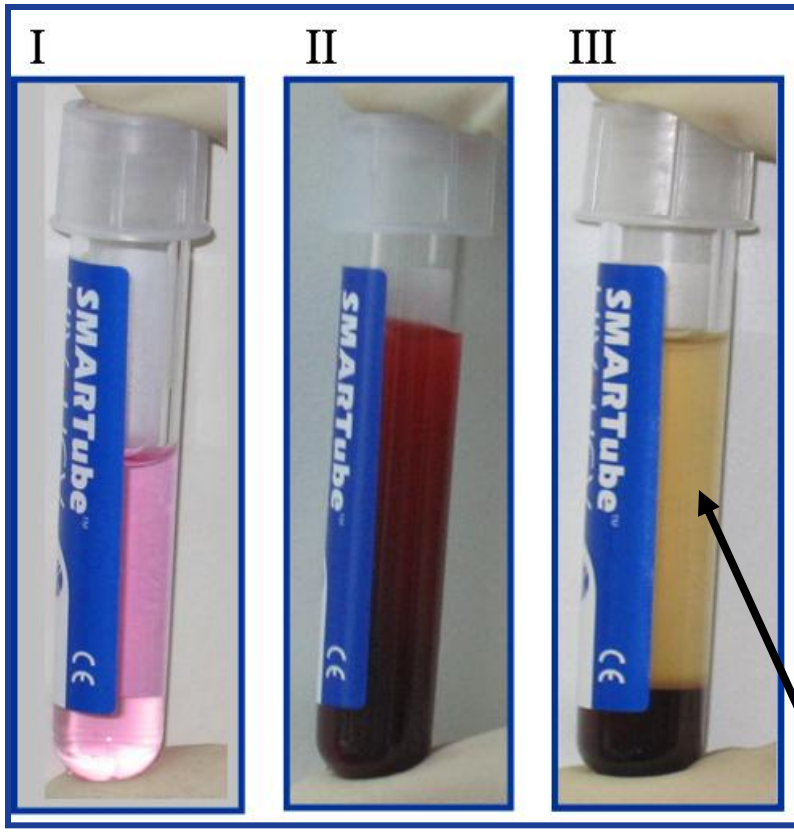
SMARTube™ with blood samples



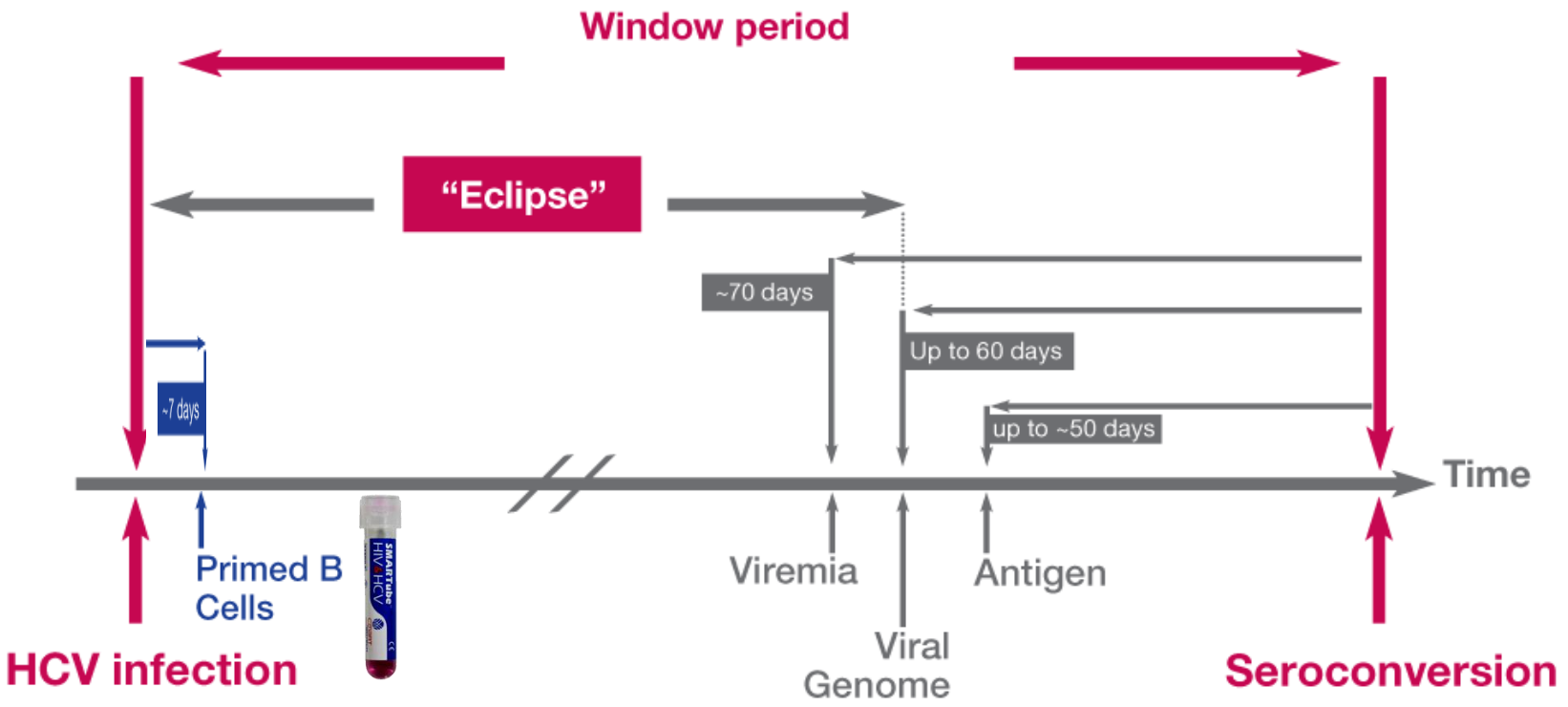
I SMARTube™ before use

II SMARTube™ containing 1 ml of whole blood sample-time 0.

III SMARTube™ after incubation.

SMARTplasma = following pre-treatment in the SMARTube

The HCV Window Period with SMARTube™



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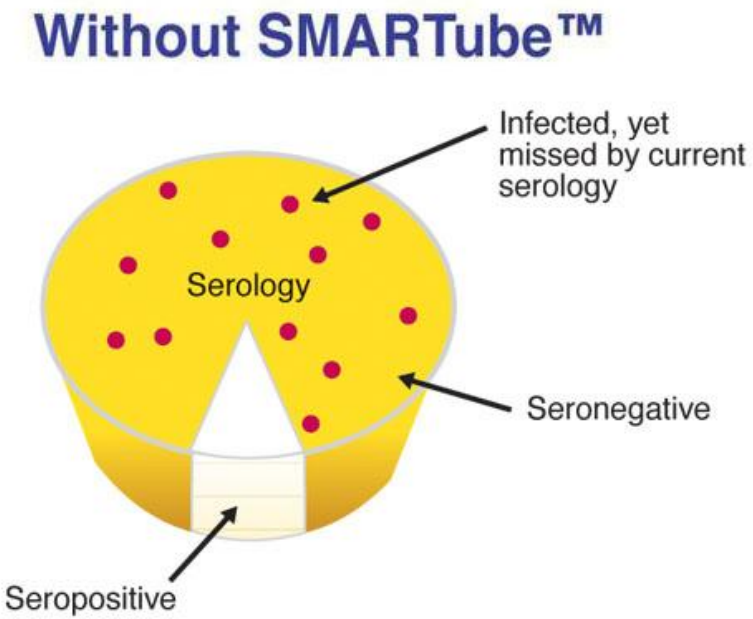
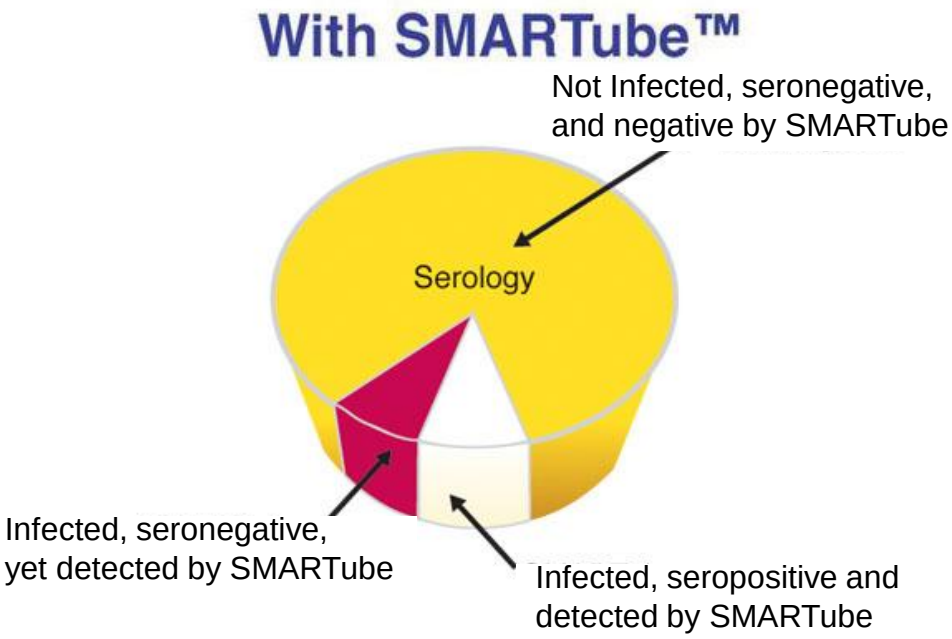
Data summary: SMARTube's effect on HCV diagnostic sensitivity

Detecting infected individuals during the seronegative window period

- 2722 high risk population
- 252 seropositives in regular serology
- 13 additional positives (252+13) after pre-treatment in the SMARTube™ - **Increased diagnostic sensitivity.**
- **Adding SMARTube to antibody testing increased HCV detection by 5.2%.**

SMARTube™ closes the Window Period – Infected people can be detected within a week from the day of infection





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Diagnosis of HCV - Challenges of antibody testing

2. **High level of false positive**, the rate changing from population to population (e.g. high rate of FP in African countries).

A major concern as it means:

I. **Epidemiologically** - over estimating prevalence

II. **Blood supply** - good blood units get discarded.

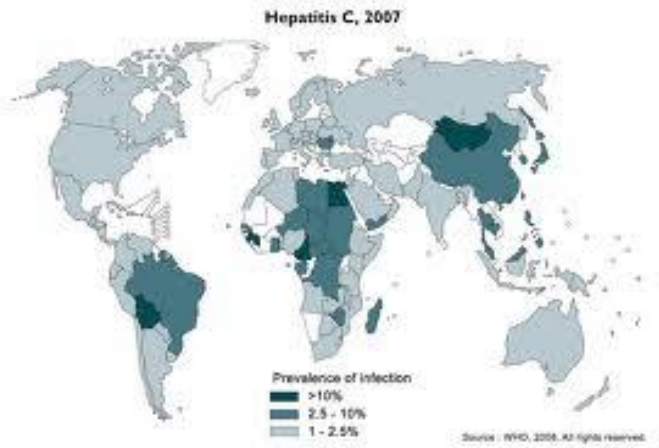
Data summary: SMARTube's effect on HCV diagnostic sensitivity

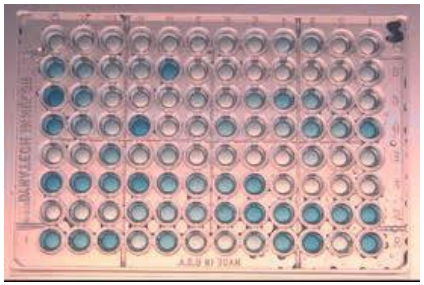
Reducing the false positive rate

- 3840 testing in routine use settings
- 27 false positives in regular serology
- 1 false positive after pre-treatment in the SMARTube™ -**Increased diagnostic specificity.**
- **96.3% reduction of false positives using the SMARTube**

Diagnosis of HCV - Challenges of antibody testing

3. **Routine antibody testing in serum does not differentiate between current / chronic infection and cleared / resolved infection**





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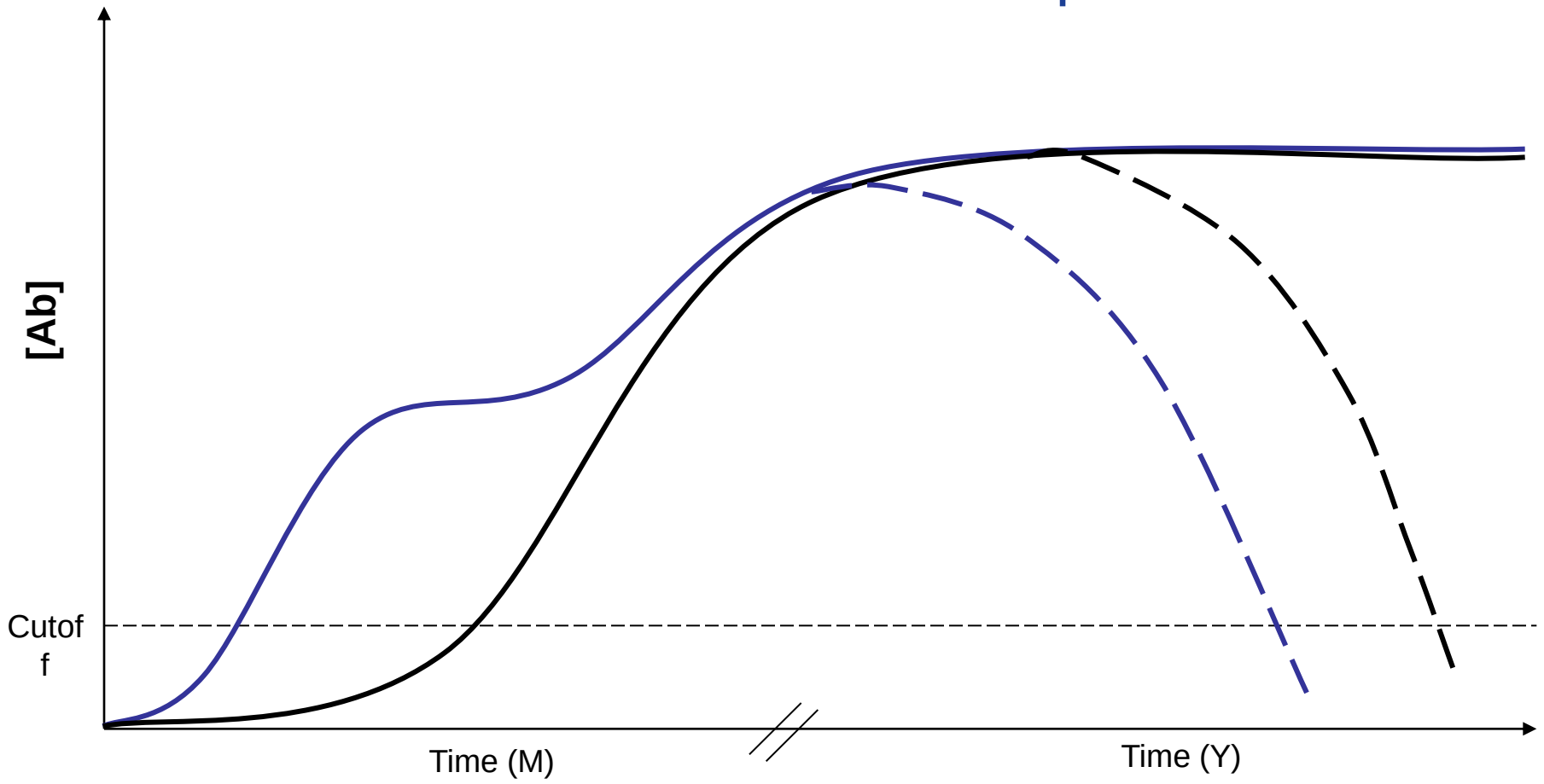
Antibodies to HCV in Plasma & SMARTplasma



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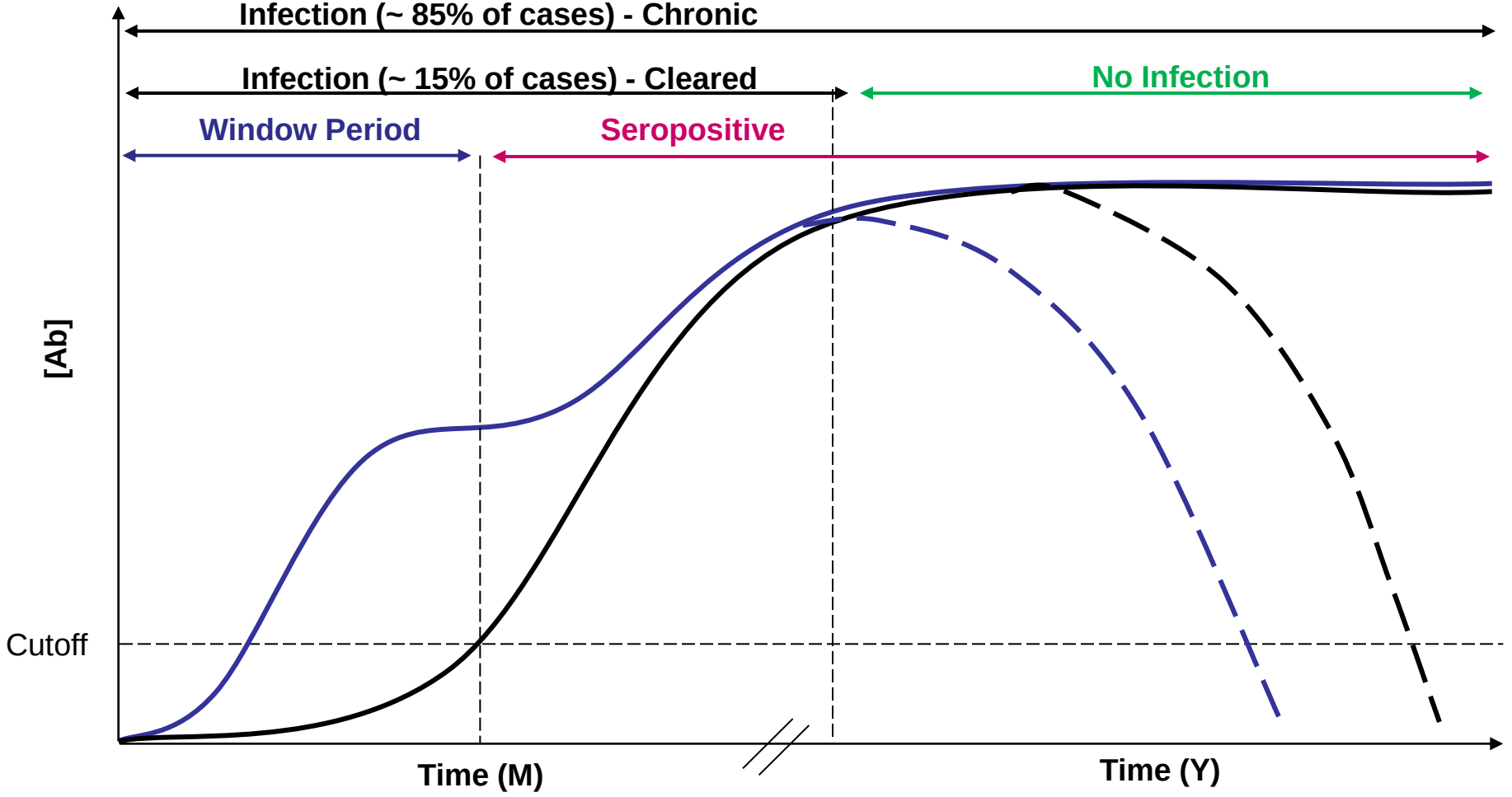
Serology versus infection status



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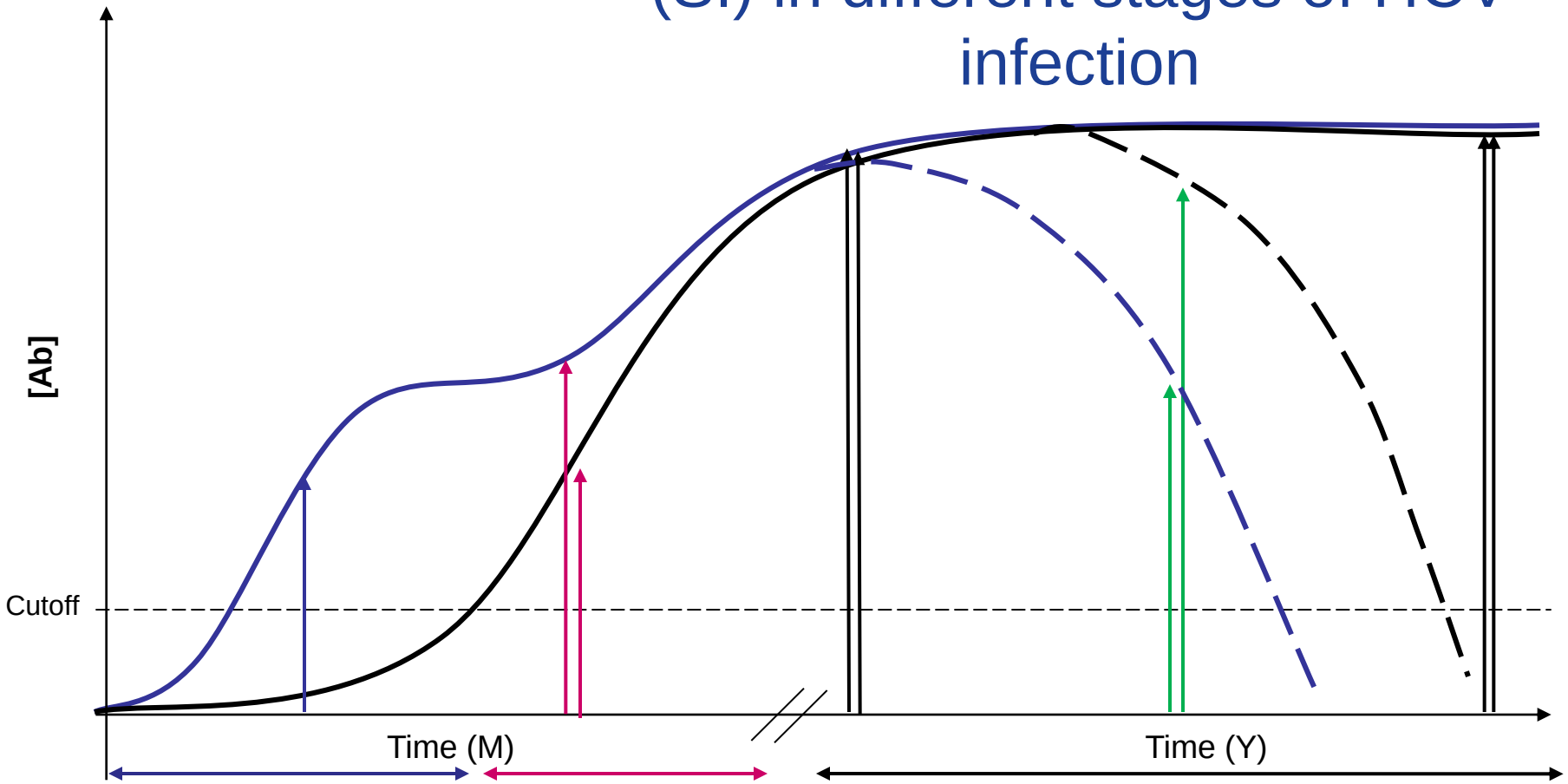
The SMARTube Stimulation Index (SI) in different stages of HCV infection



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Diagnosis of HCV by antibodies: Use of SMARTube meets the challenges

1. Long window period – enhancement of antibody production, enabling detection in the seronegative WP

2. High level of false positive – Using the SMARTube reduces the rate of false positives:
   I. Epidemiologically – True prevalence
   II. Blood supply – saving good blood from being discarded.

3. To differentiate between current/chronic infection and cleared infection – the Stimulation Index (SI) using SMARTube. (SI>1.0 = current infection, SI<1.0 = past infection)

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Embassy of Israel
Washington, D.C.

Medical Innovations from Israel

Given Imaging, Inc

Given Imaging developed the first ingestible video camera known as the PillCam®. The capsule endoscopy has become a standard practice in the majority of gastroenterologist practices.

BabySafe USA, LLC

Hisense Ltd. developed Babysense, a respiratory movement monitor that sends out an alarm if a baby stops breathing while asleep, as in SIDS (sudden infant death syndrome).

Smart Biotech Ltd.

SMART Biotech Ltd. invented SMARTube, offering the most complete detection of HIV and Hepatitis C infected individuals by enabling antibody production using a small sample of blood within days from infection. This is the only technology that enables such early detection.

Teva Pharmaceuticals

Teva Pharmaceuticals' Copaxone, a drug developed at the Weizmann Institute of Science, is prescribed by doctors worldwide as a treatment for Relapsing-Remitting Multiple Sclerosis (MS).

http://www.israelemb.org/education/publications/Science%20and%20Technology.pdf

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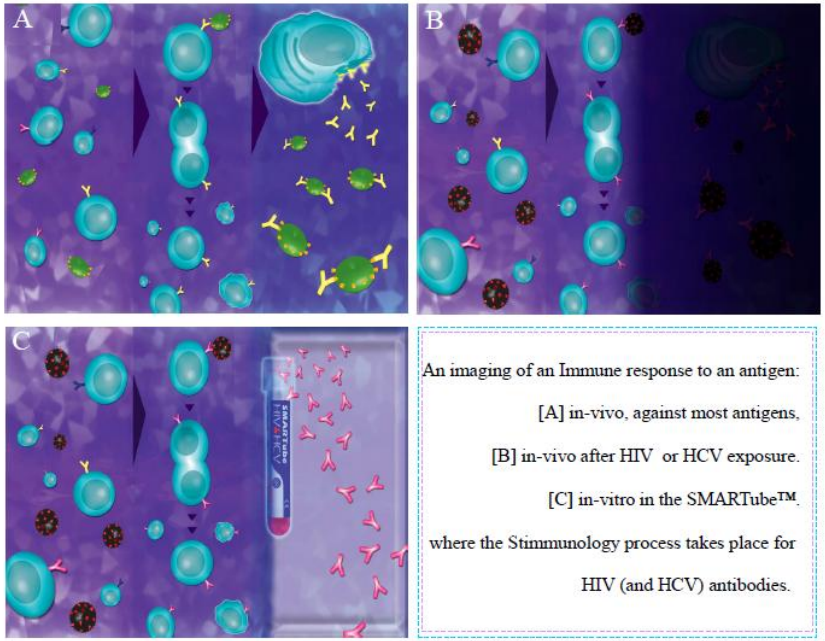
Using the SMARTube for Early and Real HCV diagnosis



An imaging of an Immune response to an antigen:
[A] in-vivo, against most antigens,
[B] in-vivo after HIV or HCV exposure.
[C] in-vitro in the SMARTube™,
where the Stimmunology process takes place for HIV (and HCV) antibodies.

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http://www.smartube-bio.com/