

# DIAGNOSIS AND MANAGEMENT OF THROMBOTIC MICROANGIOPATHY

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# CASE

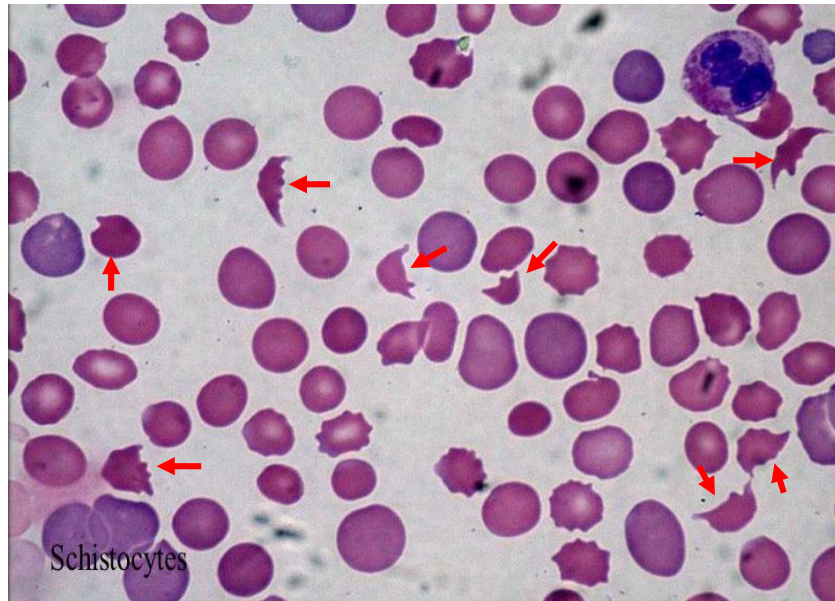
- 44 yo AAF with 3 days of h/o headache, heavy menstrual bleeding.
- She had an episode of syncope with involuntary defecation.
- She had headache and heavy menstrual bleeding.
- Also, she complained chest pain, sore throat, and fever, treated with amoxicillin x10 days at PCP office.

## CASE (CONT.)

- At ED, labs showed: H/H 6.7/20, platelet count 13, LDH 718, fibrinogen 320, D-dimer 6,644, DAT (+) for IgG, HIV rapid test (+), HBSAg (+).
- PT 13.7, PTT 30, troponin <0.01
- AST/ALT: 46/31
- Cr, 0.5

# PERIPHERAL BLOOD SMEAR:

- Numerous schistocytes and helmet cells.



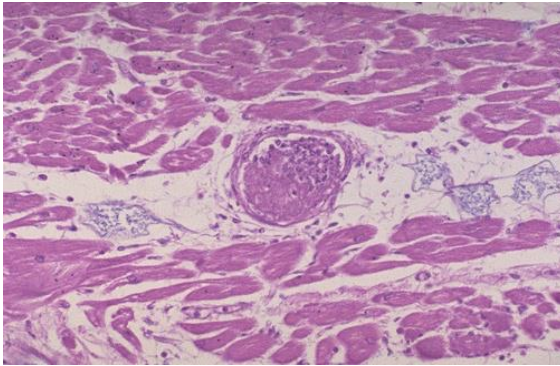
# WHAT COULD BE THE DIAGNOSIS?

**TMA, TTP and HUS?**

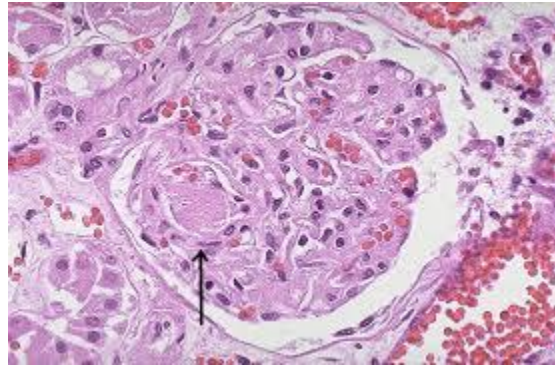
# DEFINITION OF TMA

- A pathology term, describing the presence of thrombosis in capillaries and arterioles, due to an endothelial injury

Heart



Kidney



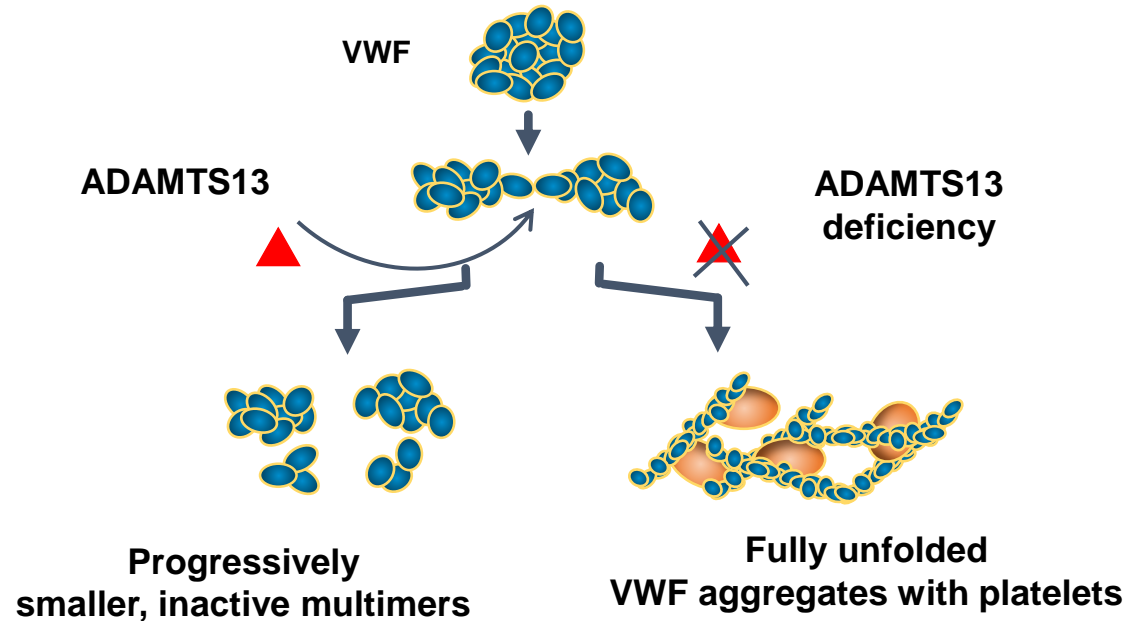
- Seen in various conditions

# TMA MAY BE ASSOCIATED WITH THE FOLLOWING CONDITIONS:

- TTP
- STEC-HUS
- aHUS
- DIC
- Malignant hypertension
- Hemolysis, Elevated Liver enzymes, Low Platelet count) (HELLP) syndrome
- Antiphospholipid antibody syndrome
- Drug toxicities (e.g. calcineurin inhibitor)

# Mechanism of TTP

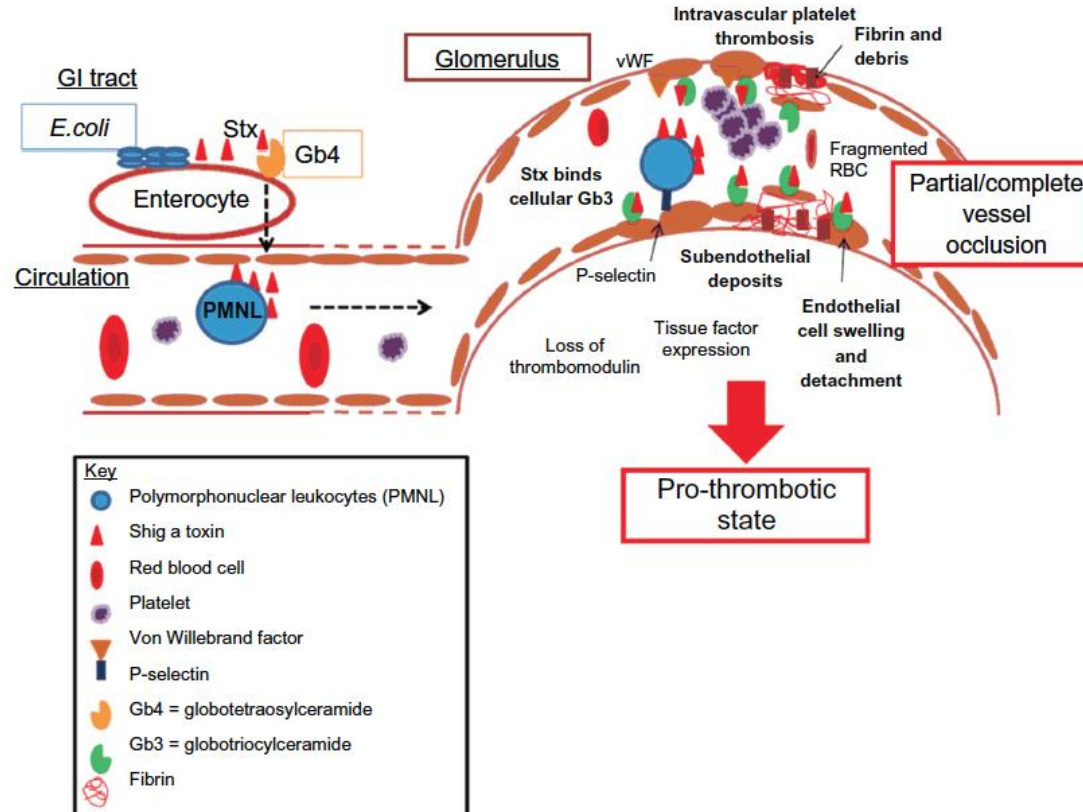
Insufficient ADAMTS13 activity (<5%)  
leaves von Willebrand factor intact



Suppress/remove inhibitor autoantibody;  
replace ADAMTS13

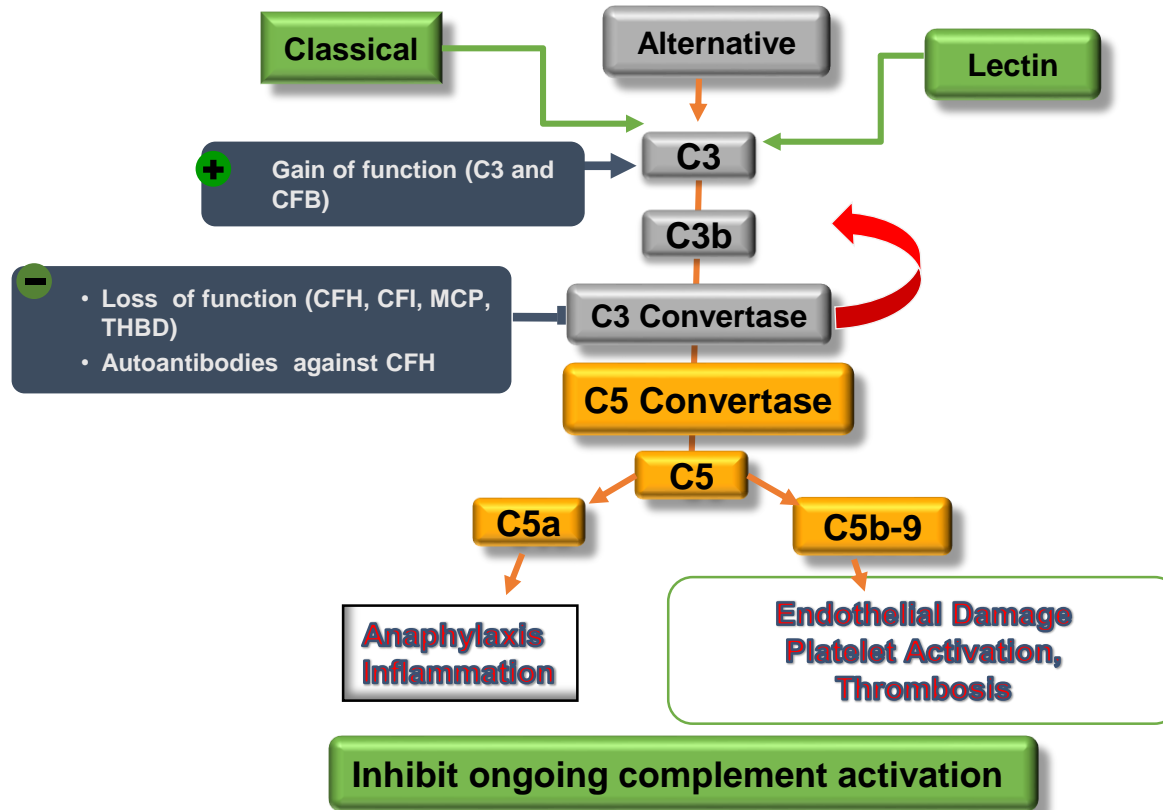


# MECHANISM OF STEC-HUS

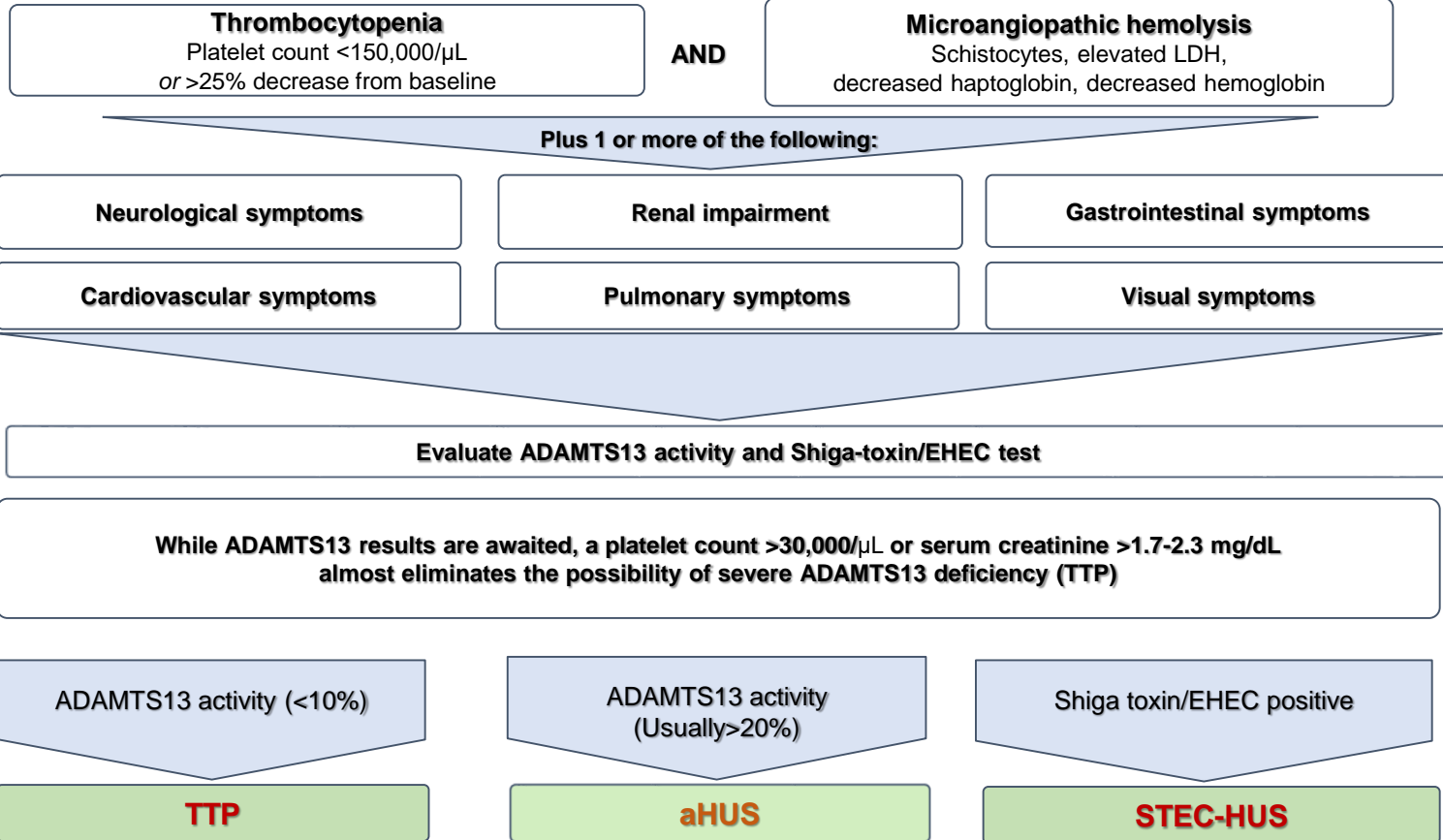


# MECHANISM OF ATYPICAL HUS

Genetic defects lead to chronic uncontrolled activation of the complement system



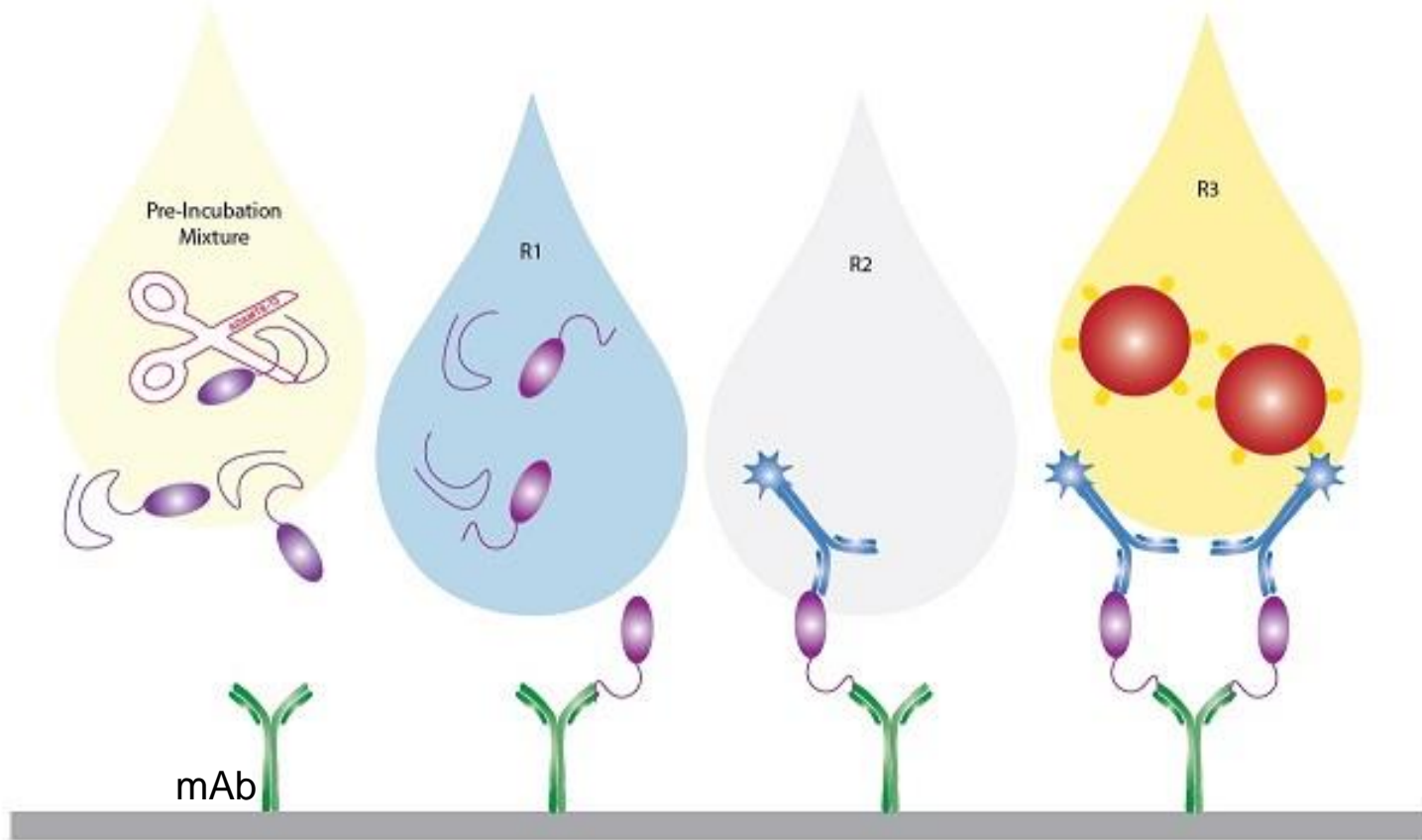
# CLINICAL DIFFERENTIAL DIAGNOSIS



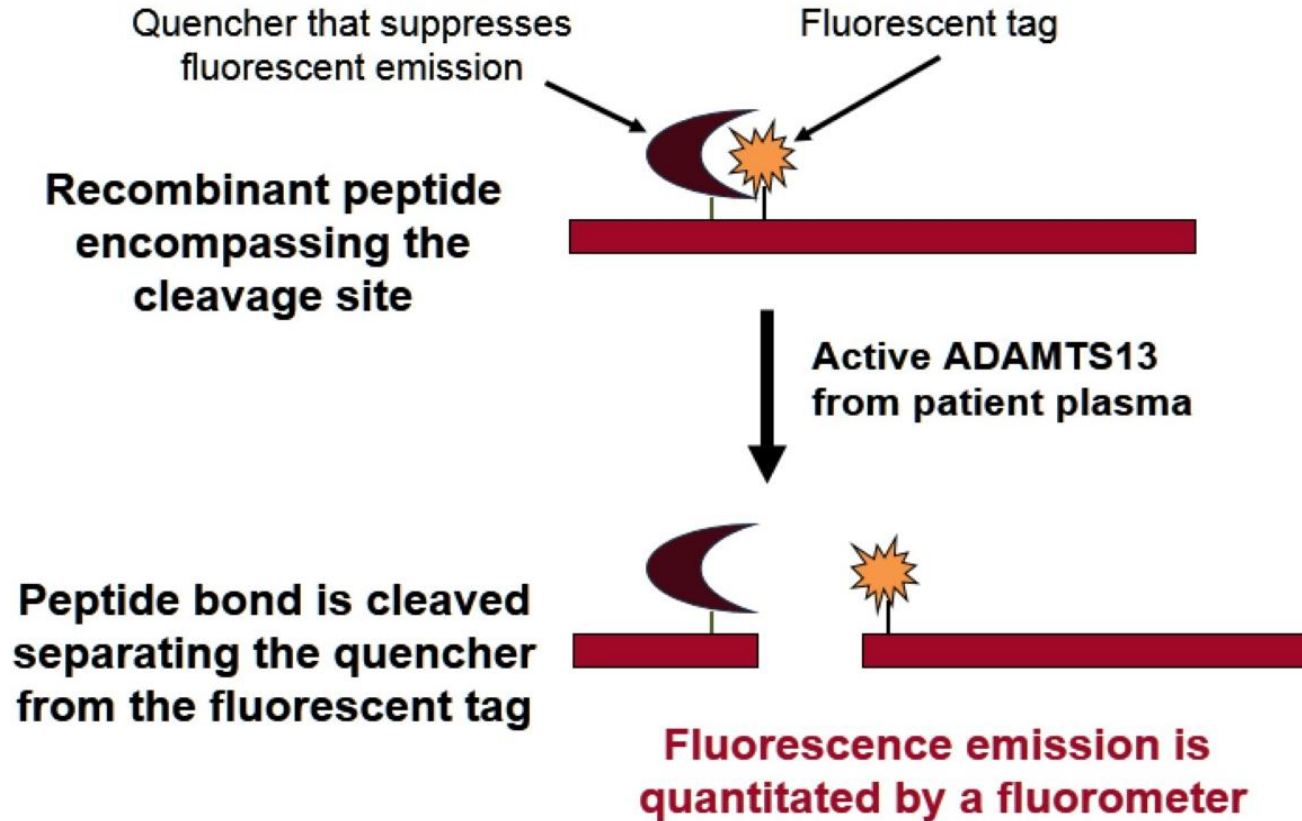
# HOW TO TEST ADAMTS13 ACTIVITY?

- Screening activity assay
- FRETs-VWF73 activity assay
- Chromogenic ELISA activity assay
- Fluorogenic activity assay
- ADAMTS13 antigen assay
- Anti-ADAMTS13 IgG assay

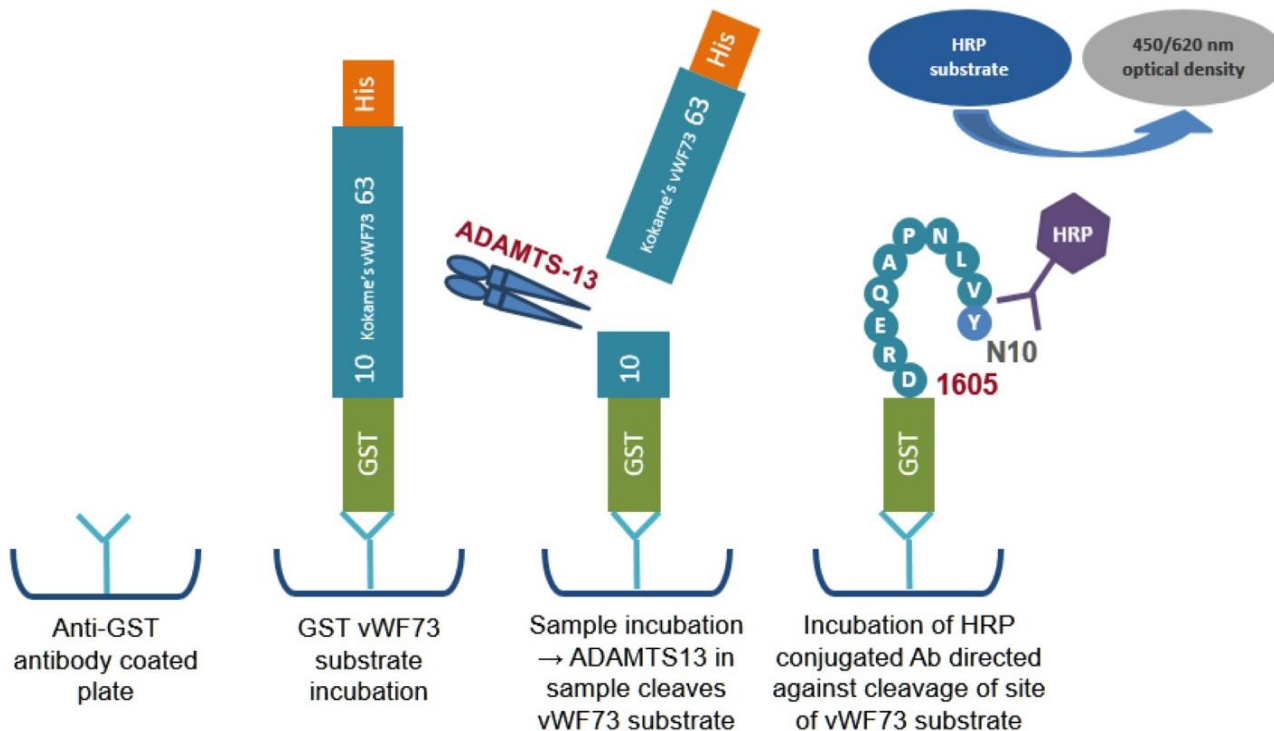
# TECHNOSCREEN® ADAMTS-13 ACTIVITY



# FLUORESCENT ENERGY RESONANCE TRANSFER (FRET) ASSAY

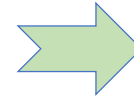


# CHROMOGENIC ELISA-BASED ADAMTS13 ACTIVITY ASSAY



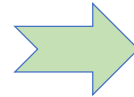
# HOW TO INTERPRET THE RESULTS?

- ADAMTS13 activity <10% or 10 U/dL  
Inhibitor >0.4 U/mL (positive)



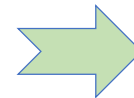
Immune-mediated  
TTP (iTTP)

- ADAMTS13 activity <10% or 10 U/dL  
Inhibitor <0.4 U/mL (Negative), but  
Anti-ADAMTS13 IgG > 15 U/mL



Immune-mediated  
TTP (iTTP)

- ADAMTS13 activity <10% or 10 U/dL  
Inhibitor <0.4 U/mL (Negative)  
Anti-ADAMTS13 IgG < 15 U/mL or  
ADAMTS13 mutation test (positive)



Hereditary or  
congenital  
TTP (cTTP)



# MANAGEMENT OF TMA

**cTTP:** Plasma infusion,  
Factor VIII concentrate  
Recombinant ADAMTS13  
Gene therapy

**iTTP:** Therapeutic plasma exchange  
Corticosteroids/Vincristine/Cytosan  
Rituximab  
Caplacizumab  
Recombinant ADAMTS13

**aHUS:** Eculizumab

# TAKE HOME MESSAGE

- TTP and aHUS are two distinct prototypes of TMA.
- Clinical parameters + ADAMTS13 are essential for differential diagnosis
- Plasma exchange, steroids, rituximab, and caplacizumab are for iTTP, but eculizumab for aHUS.
- Further investigation is necessary to understand the pathogenesis of other types of TMA.