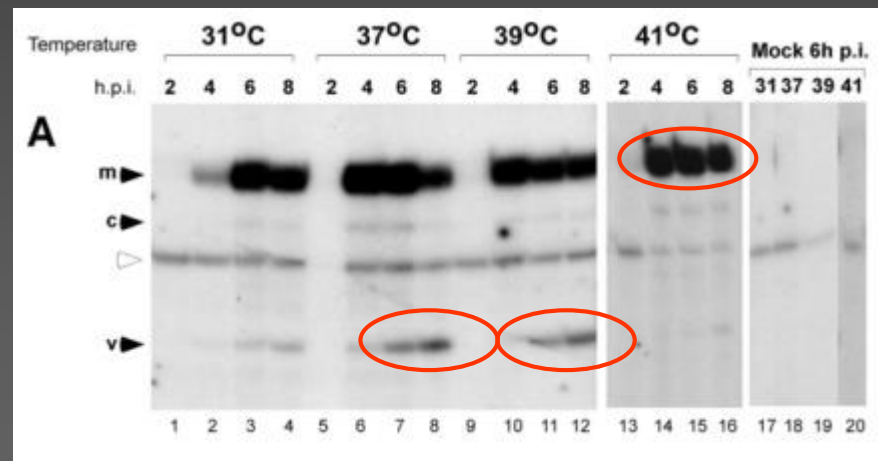
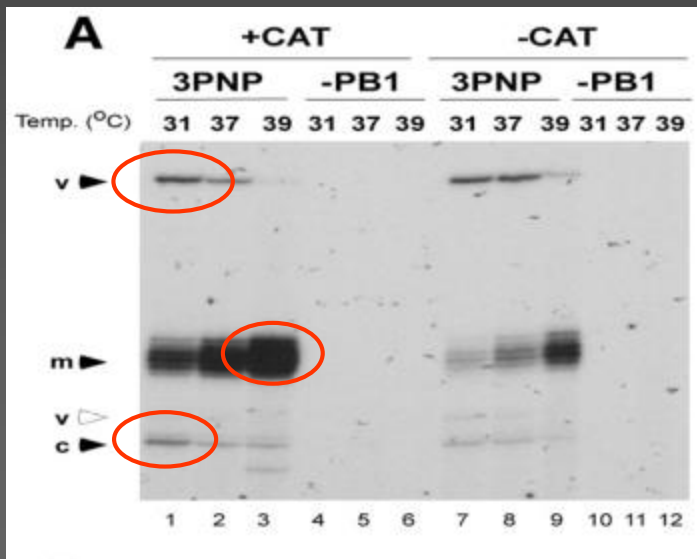


*Dalton et al. (Paul Digard group) Virology Journal 2006, 3:58*

“... the ‘switch’ that regulates the transition from transcription to replication is poorly understood.”

“Temperature strongly affects the balance between plus and minus-sense RNA synthesis with high temperature causing a large decrease in vRNA accumulation, a moderate decrease in cRNA levels but (depending on genome segment) either increased or unchanged levels of mRNA.”

**Conclusion:** “The differential stability of negative and positive sense polymerase-promoter complexes explains why **high temperature favours transcription over replication.**”



transcription

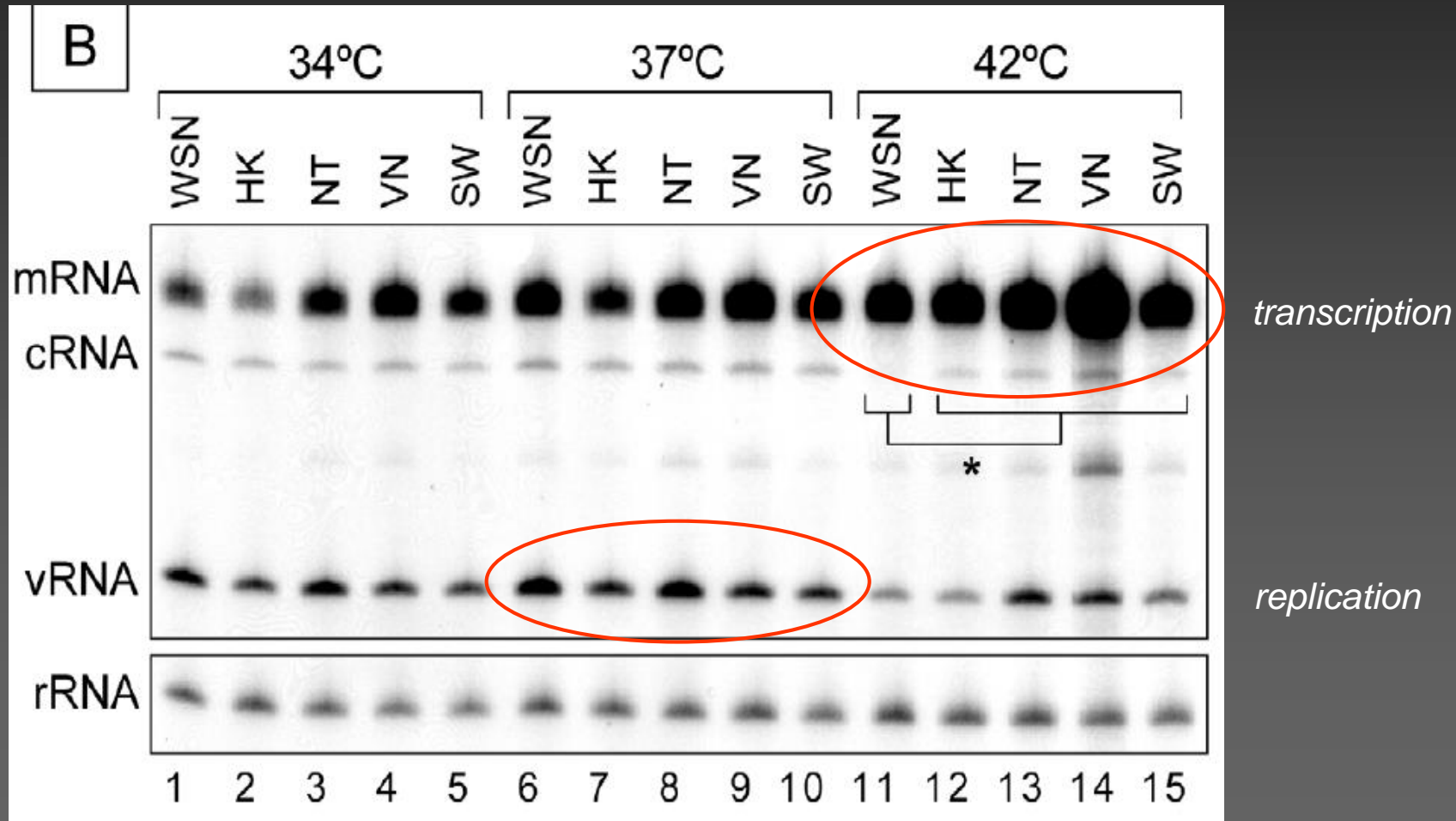
replication

A/PR/8/34 virus (80 yrs)

Kashiwagi *et al.*, (2010). PloS one, 5(12), e15140.

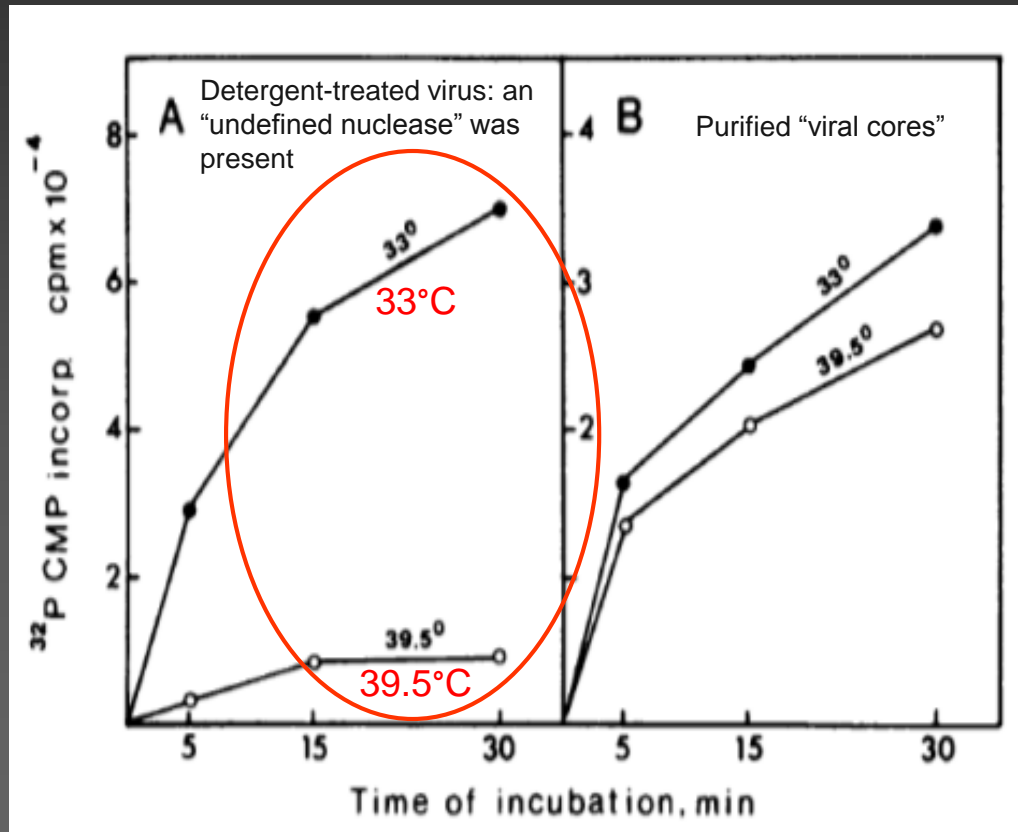
High temperature favours transcription over replication.

A/ WSN/33 (H1N1 Spanish flu)  
A/HongKong/156/97 (H5N1 bird flu)  
A/NT/60/68 (H3N2 Hong Kong flu)  
A/Vietnam/1194/04 (H5N1 bird flu)  
A/Kurume/K0910/2009 (H1N1 swine flu)

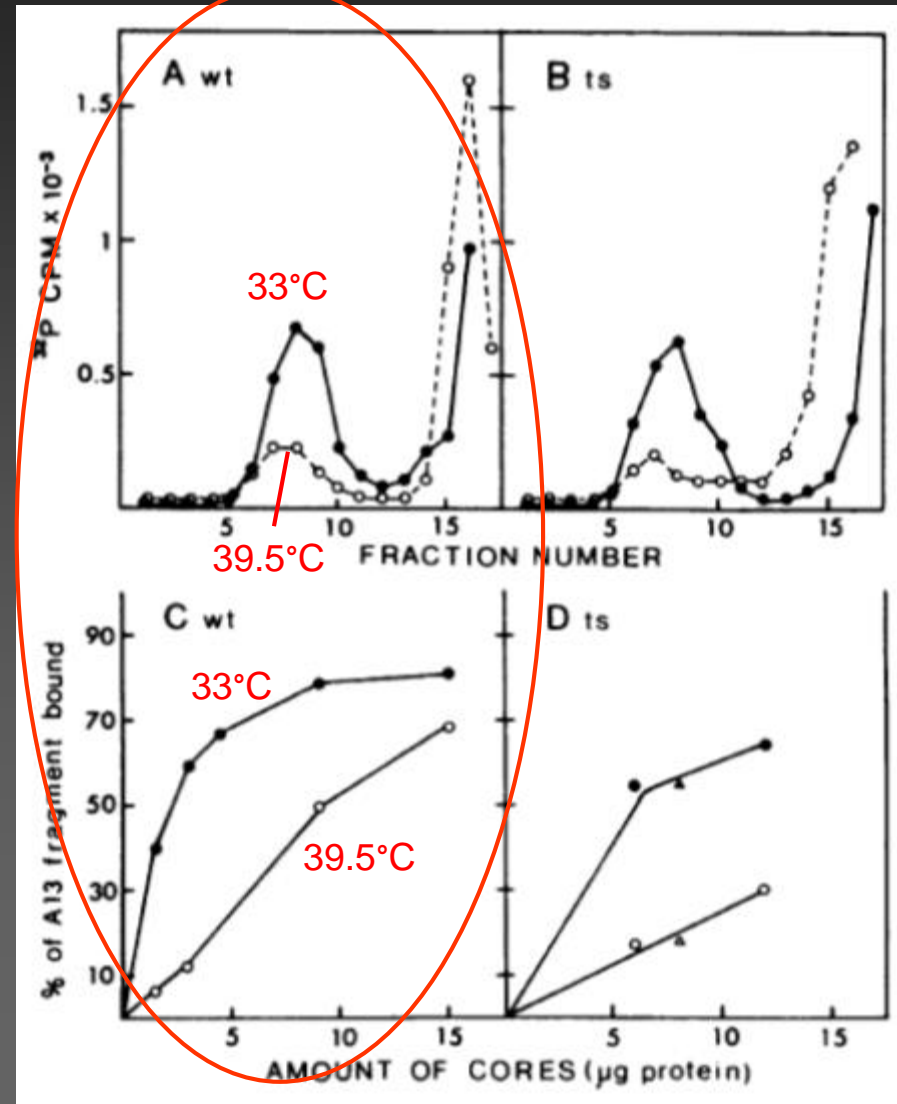


Ulmanen et al. (1983). Journal of virology, 45(1), 27-35.

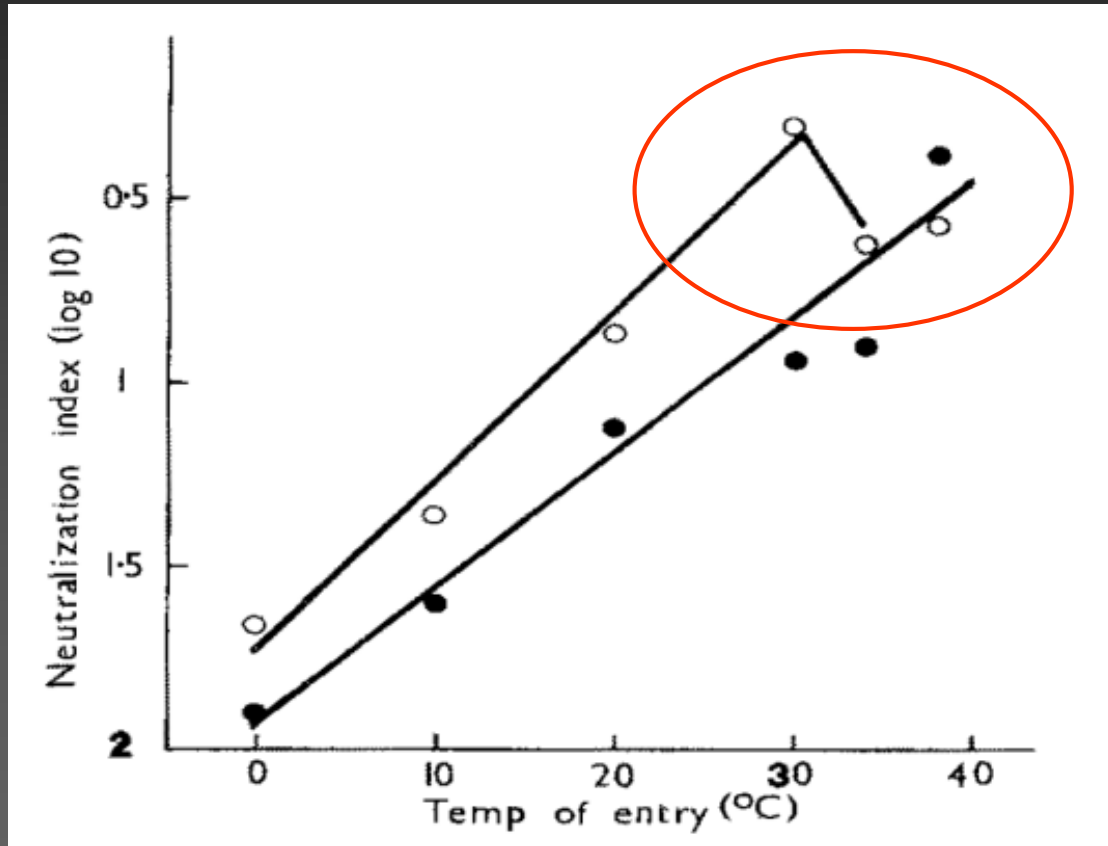
### *In vitro* transcription (WSN 1933)



### *Binding of primer for transcription*



Russell, P., Newcastle Disease Virus and Two Influenza Viruses: Differing Effects of Acid and Temperature. Archives of Virology 88, 159--166 (1986)



### *Entry into cells*

“At 34 °C and 38° C less A/Jap/Bel escaped neutralization by MAb than at 30 °C (Fig. 2). This was repeated on two separate occasions using a chicken anti-H2 serum **when 100% of virus escaped neutralization at 30°C as compared to 50 per cent at 38°C.**”

# Naturally-occurring *ts* viral strains

**Rhinoviruses** were first isolated at 35°C but a greater variety of rhinoviruses was discovered at 33°C [41], and this is the temperature that is recommended today for their isolation [42].

**Coronaviruses** were first isolated at 33°C [38] although laboratory strains are now frequently propagated at 37°C.

In 1962 Stern and Tippett [43] collected four viral specimens from patients with **H2N2 “Asian” influenza**, all of which were *ts*. All four isolates gave cytopathic effects in monkey cells and agglutination in eggs at 33°C but not at 37°C. The authors also found that (in 1962) **FM1** and **PR8** grew more slowly in monkey cells at 37°C than at 33°C.

In 1977, Kung *et al.* found that nine of ten isolates of the newly emerged “Russian” **H1N1 influenza** were *ts* [44].

Oxford *et al.* found that 17 of 26 recent **H1N1** isolates, and 2 of 11 recent **H3N2** isolates were *ts*, producing at least 10 times more viral plaques at 34°C than at 38.5°C [24].

Chu tested seven **H1N1** strains with varying degrees of temperature sensitivity in volunteers and found a correlation between temperature sensitivity and the severity of VRTI symptoms [23].