



# Adenovirus mediated IFN- $\gamma$ expression in cutaneous lymphomas: monitoring of local and systemic events

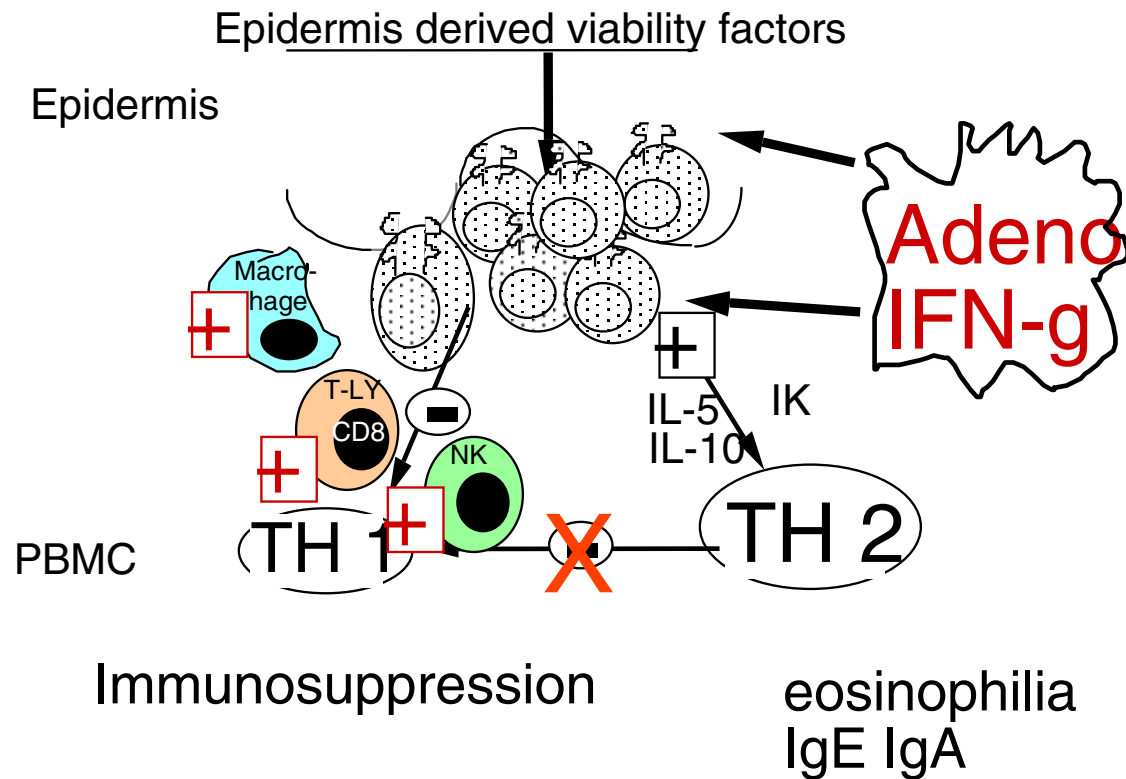
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S. Eichmüller, M. Urosevic



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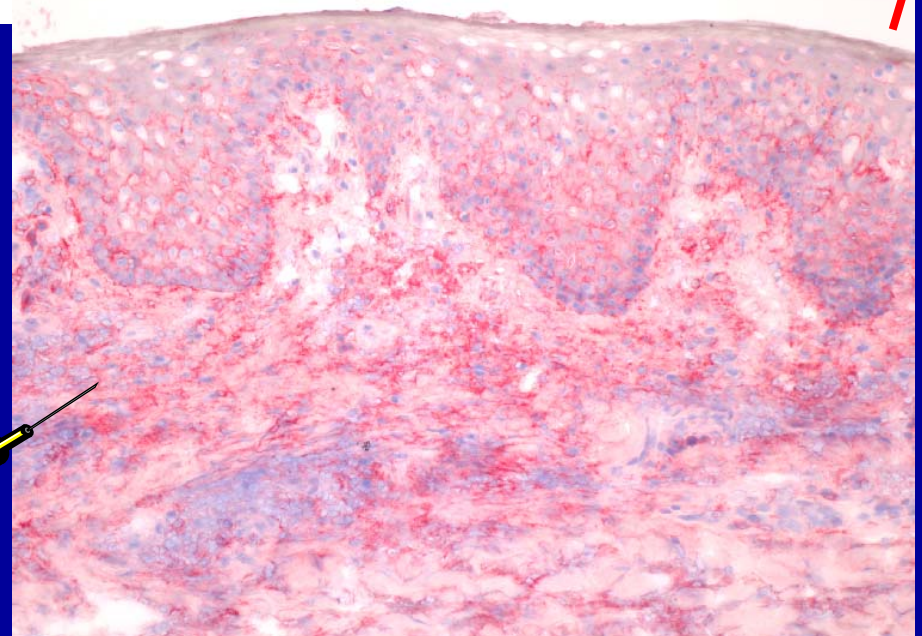
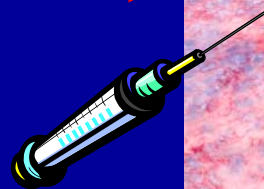
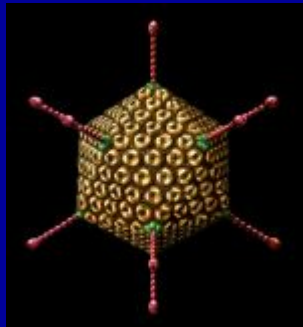
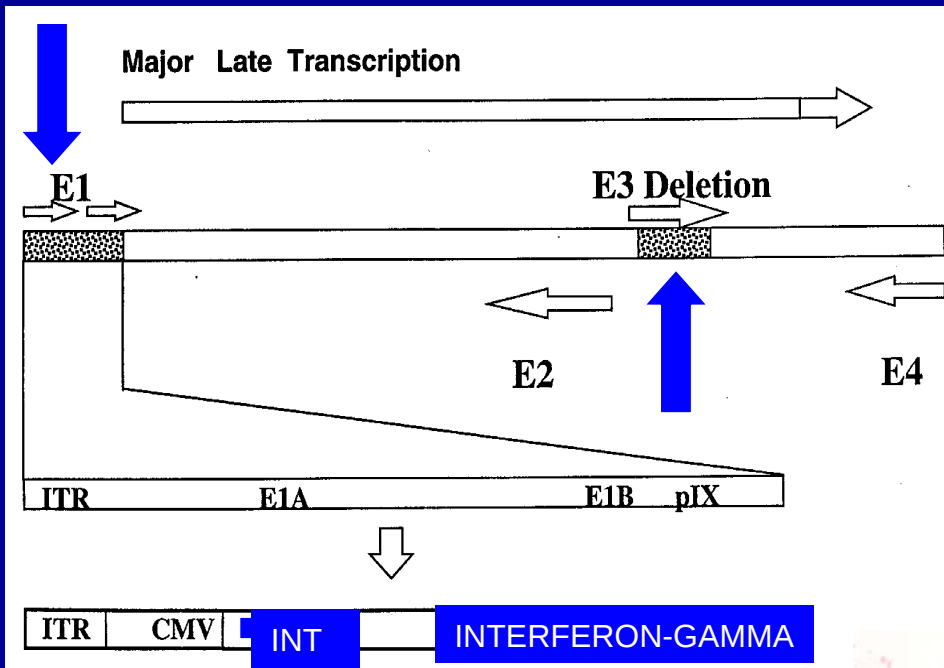
# Immune intervention in MF using a third generation adenoviral vector system



The vector:  
Adeno-IFN- $\gamma$   
TG1042 (Transgene)

Local IFN- $\gamma$  production

The recipients:  
H-CAR expression in CTCL



# TG1042.01 : Cutaneous Lymphomas

Phase I:

TNM stage Ib or higher

Failure of local tumor control by at least 2 first line treatments

Dose-Escalating

3 Dose levels:  $3 \times 10^9$ ,  $3 \times 10^{10}$ ,  $3 \times 10^{11}$  tp

3 Patients / dose level

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Adenovirus-mediated intralesional interferon- $\gamma$  gene transfer induces tumor regressions in cutaneous lymphomas

Reinhard Dummer, Jessica C. Hassel, Friederike Fellenberg, Stefan Eichmüller, Tanja Maier, Philippe Slos, Bruce Acres, Pascal Bleuzen, Vincent Bataille, Patrick Squiban, Günter Burg, and Mirjana Urošević

$3 \times 10^{11}$  tp 12 additional patients March 2002- Sept. 2004

## Inclusion criteria:

Histologic proof of CTCL or CBCL

Performance status 0,1 or 2 on the ECOG scale

TNM stage Ib or higher

at least 2 first-line treatments

No systemic chemo- or immunotherapy within preceding 3 weeks

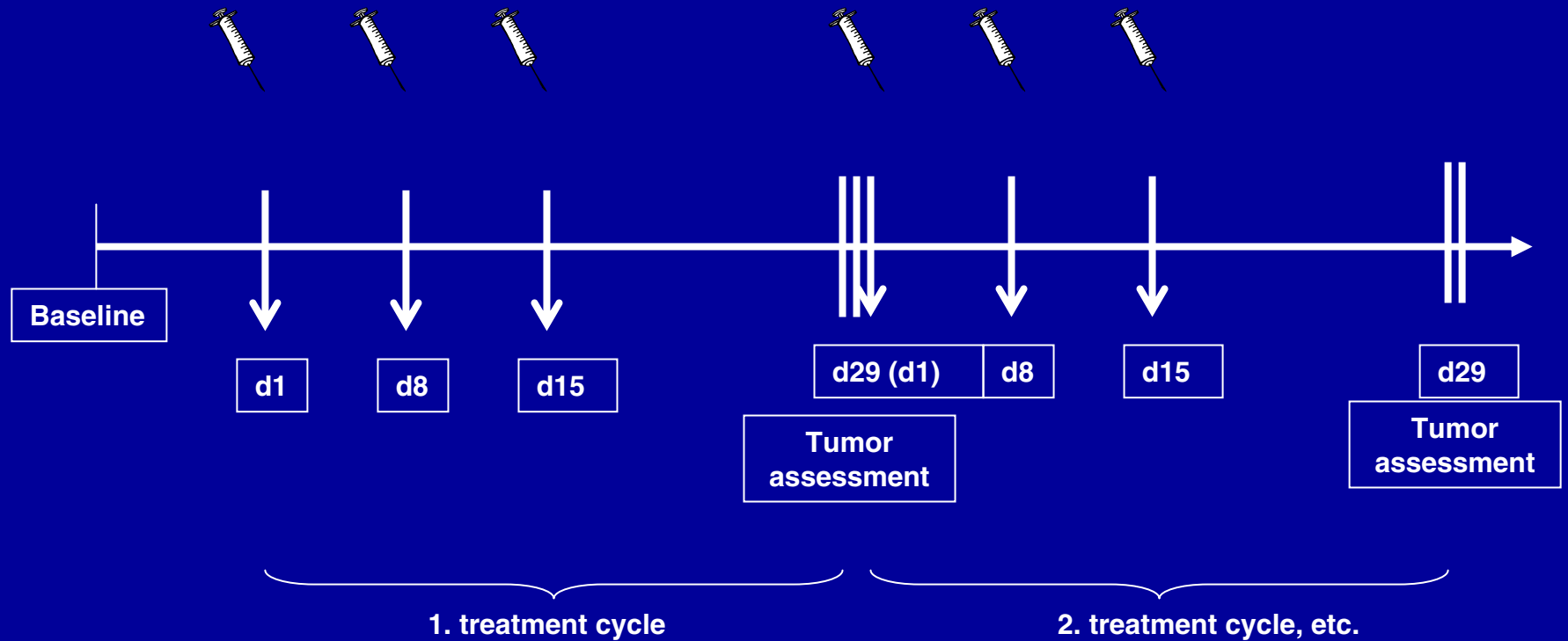
Minimum life expectancy > 3 months

Adequate hematologic, hepatic and renal function

## Exclusion criteria:

- HIV+ or other active systemic infections
- Serious concomitant systemic medical disorders
- Concomitant corticosteroid therapy
- Major surgery in previous 3 weeks
- Pregnancy
- Other therapies for lymphoma

# Treatment plan



# Side effects

Adeno-IFN- $\gamma$

Mainly locally: erythema,  
oedema, pain

Flu-like symptoms: chills and  
fever, head-ache, dizziness

Fatigue

Flushing

No relevant changes in routine  
laboratory values

No SAEs nor Grade 3/4  
toxicities



before



after  
1st injection



after  
2nd injection

# Outcome/Response

OR: 11/20    3/12    8/17

| Patient | Age | Sex | DG         | Stage | Dose (tp) | No. of injections | Response I.L.                    | Response non I.L. | Response overall | Response duration |
|---------|-----|-----|------------|-------|-----------|-------------------|----------------------------------|-------------------|------------------|-------------------|
| #001    | 84  | M   | MF         | Ib    | 3·10E+9   | 9                 | PR                               | SD                | PR               | 6 mo              |
| #002    | 66  | F   | MF         | IIa   | 3·10E+9   | 12                | CR                               | CR                | CR               | 1 mo              |
| #003    | 25  | M   | MF         | Ib    | 3·10E+9   | 12                | SD                               | SD                | SD               | n.e               |
| #004    | 44  | F   | MF         | IIb   | 3·10E+10  | 3                 | SD                               | PD                | PD               | n.e               |
| #005    | 46  | M   | SS         | III   | 3·10E+10  | 9                 | SD                               | SD                | SD               | n.e               |
| #006    | 39  | F   | LyP        | n.a.  | 3·10E+10  | 5                 | CR                               | CR                | CR               | 3 mo              |
| #007    | 67  | M   | SS         | III   | 3·10E+11  | 3                 | SD                               | SD                | SD               | n.e               |
| #008    | 34  | M   | MZL        | n.a.  | 3·10E+11  | 9                 | PR                               | n.e.              | n.e.             | 5 mo              |
| #009    | 34  | M   | FCCL       | n.a.  | 3·10E+11  | 3                 | CR                               | SD                | PR               | 1 mo              |
| #010    | 59  | M   | FCCL       | n.a.  | 3·10E+11  | 3                 | CR                               | n.a.              | CR               | 14 mo             |
| #011    | 87  | F   | MF         | IIb   | 3·10E+11  | 14                | n.e                              | n.e.              | n.e.             | n.e               |
| #012    | 58  | M   | FCCL       | n.a.  | 3·10E+11  | 2                 | treatment interrupted due to SAE |                   |                  | n.e               |
| #013    | 46  | M   | CD30+ LTCL | IIb   | 3·10E+11  | 3                 | CR                               | n.a.              | CR               | 3 mo              |
| #014    | 55  | M   | CD30- LTCL | IIb   | 3·10E+11  | 3                 | SD                               | PD                | PD               | n.e               |
| #015    | 55  | M   | LyP        | n.a.  | 3·10E+11  | 12                | PR                               | SD                | PR               | 5 mo              |
| #016    | 66  | F   | CD30+ LTCL | IIa   | 3·10E+11  | 12                | CR                               | n.a.              | CR               | 9 mo +            |
| #017    | 31  | M   | GSS        | IIb   | 3·10E+11  | 15                | PR                               | n.a.              | SD               | ongoing           |
| #018    | 93  | F   | MF         | IIb   | 3·10E+11  | 12                | SD                               | SD                | SD               | n. e.             |
| #019    | 49  | M   | CD30+ LTCL | IIb   | 3·10E+11  | 6                 | SD                               | SD                | SD               | 6 mo +            |
| #020    | 54  | M   | CD30+ LTCL | IIb   | 3·10E+11  | 3                 | CR                               | n.a.              | CR               | 6 mo +            |

# PUVA resistant CD30+ CTCL



3 months later



9 months later

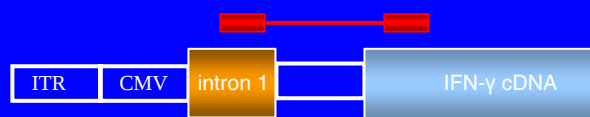


# Mycosis fungoides

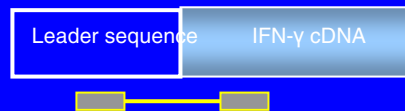
before after 9 injections



# Primer design for vector encoded vs. endogenous IFN- $\gamma$

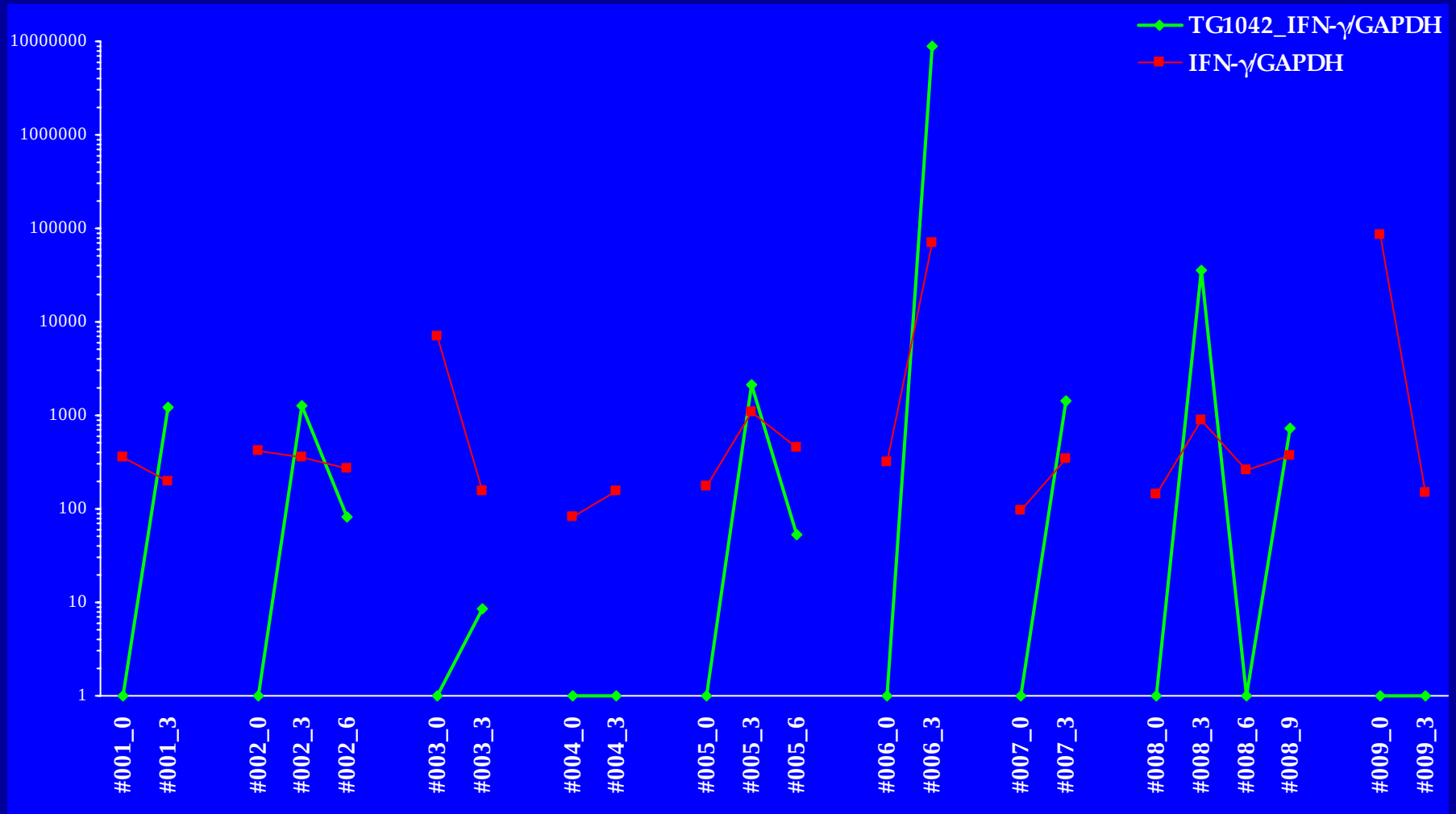


TG1042-derived IFN- $\gamma$   
primers

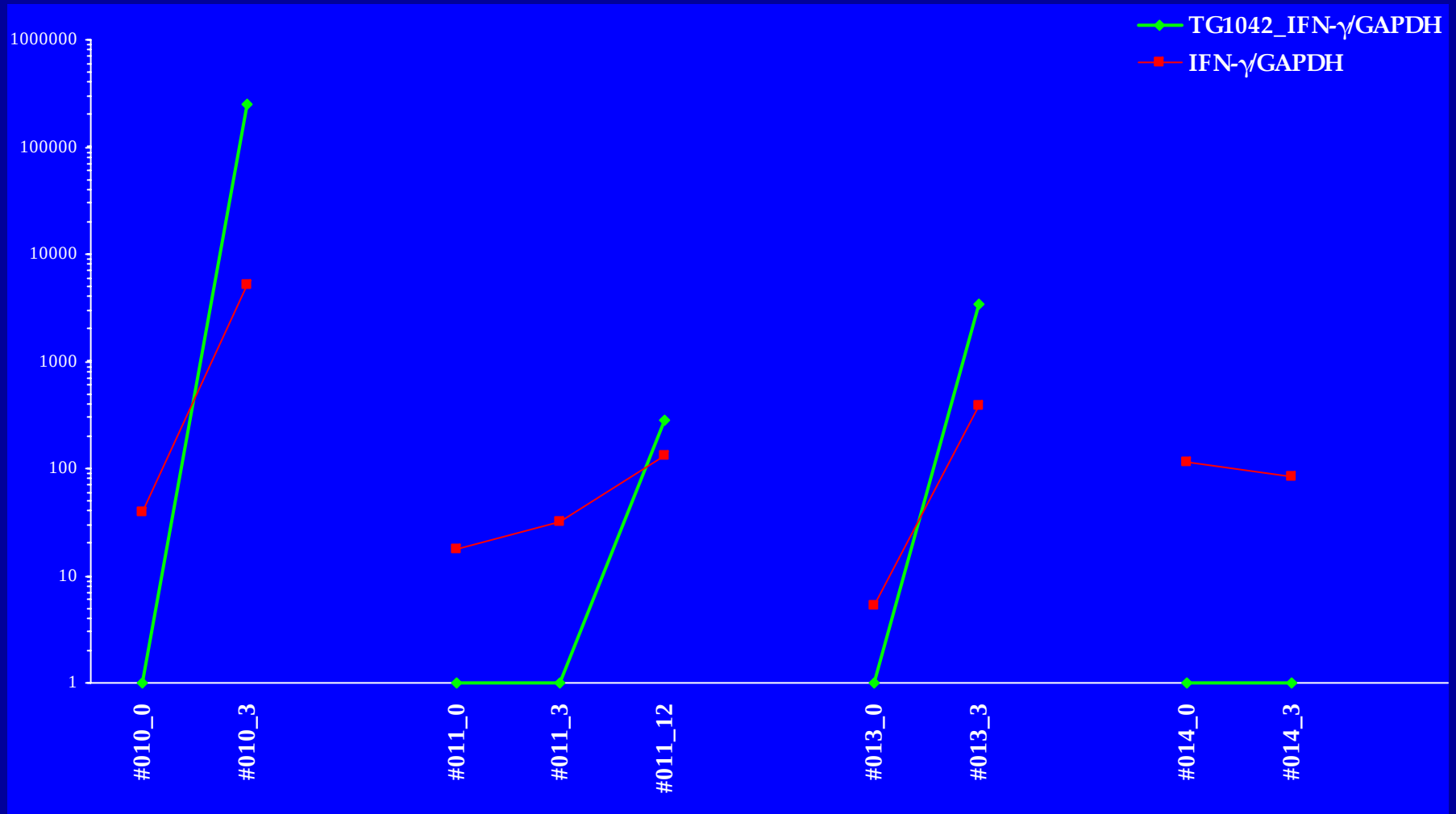


endogenous IFN- $\gamma$   
primers

# TG1042-derived IFN- $\gamma$ and endogenous IFN- $\gamma$



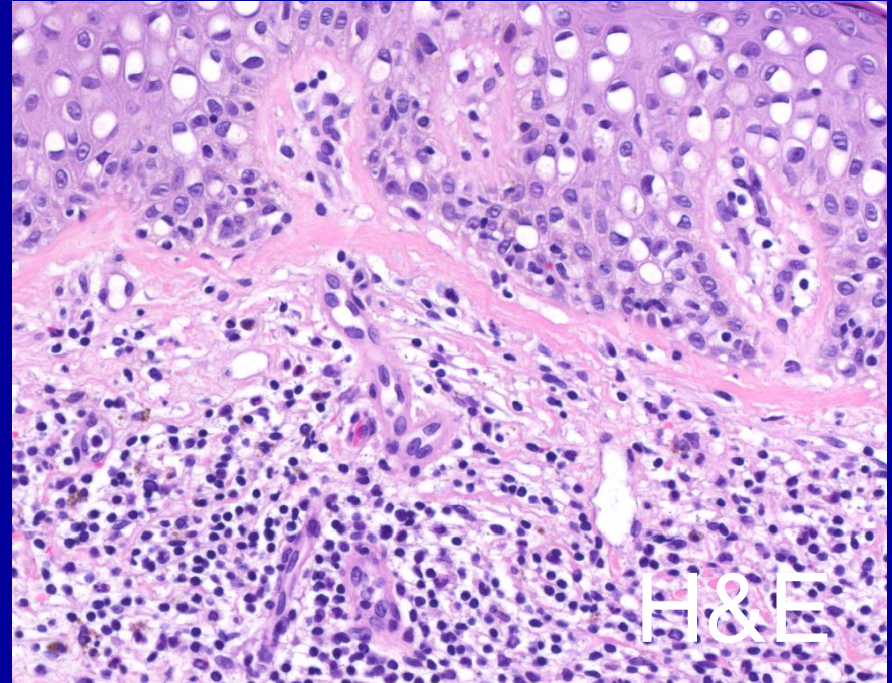
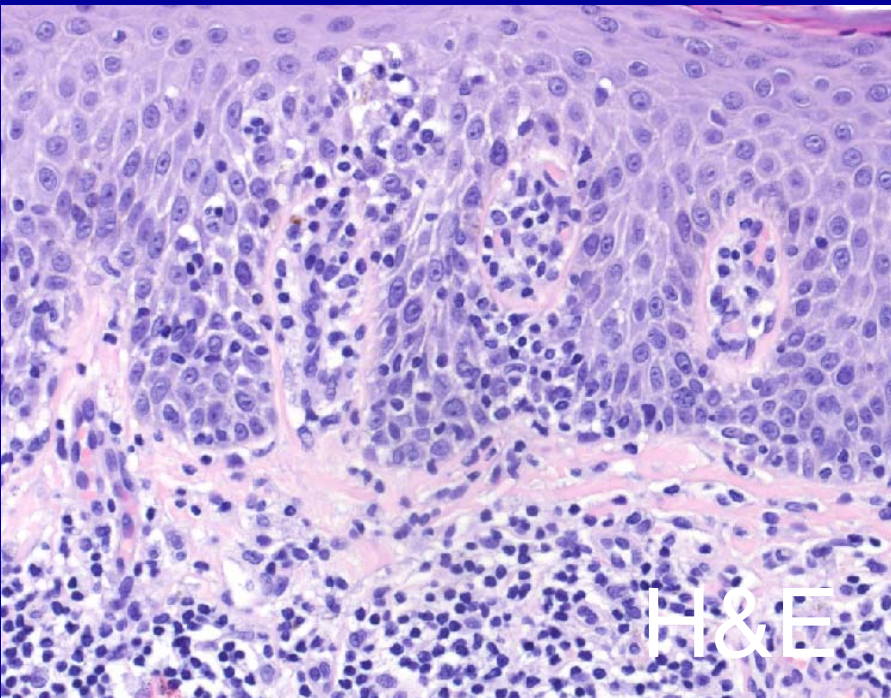
# TG1042-derived IFN- $\gamma$ and endogenous IFN- $\gamma$



# Mycosis fungoides

before

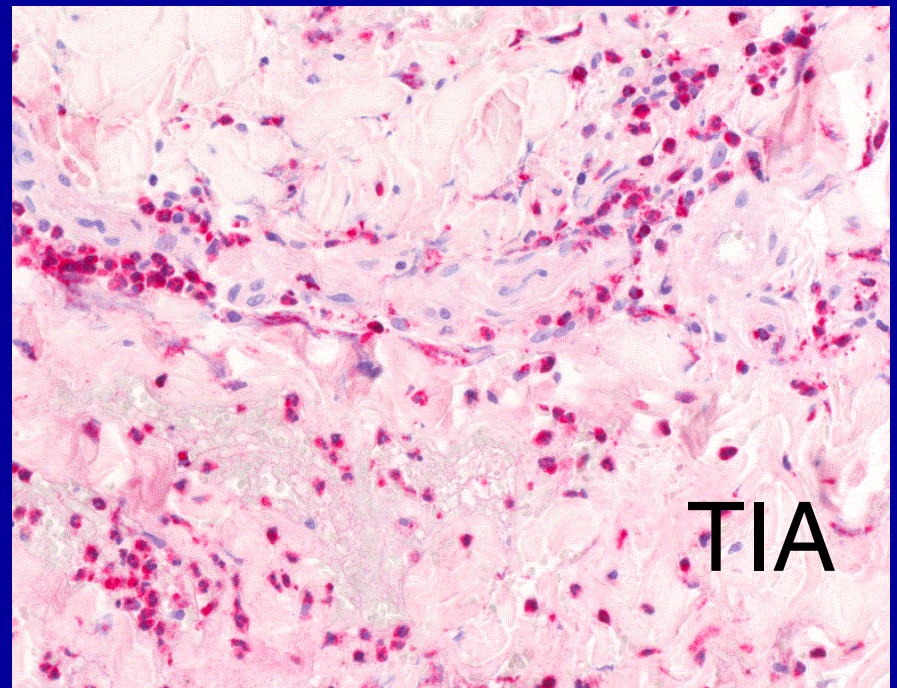
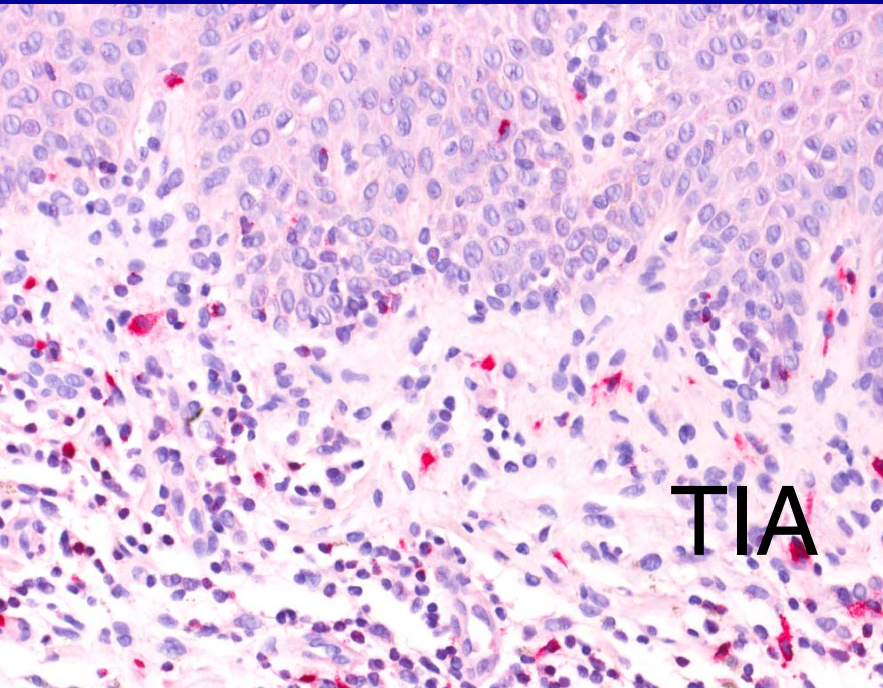
after



# Mycosis fungoides

before

after



# CBCL

before

after 3

Injections

