Multidisciplinary Investigation of FOXP1 Deletion Case Study

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INTRODUCTION

The transcription factor Forkhead box protein 1 (FOXP1) is implicated in the development of multiple organ systems. While murine models have demonstrated that FOXP1 is an essential regulator of macrophage, B and T cell development, reports describing the immunologic phenotype in human subjects with 3p13 deletion are exceedingly sparse.

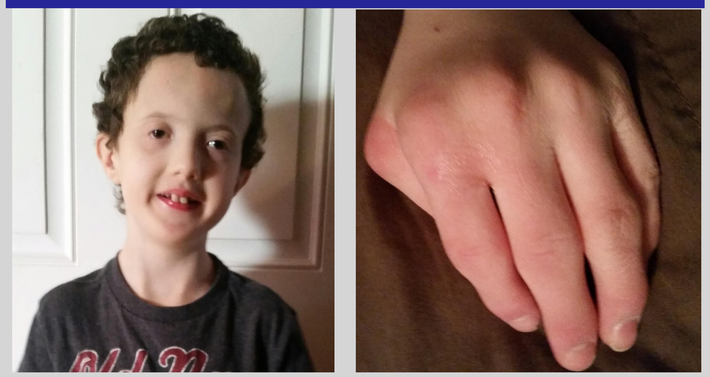
CASE PRESENTATION

An 11-year-old Caucasian male with 3p12.3-3p14.1 deletion features of autism and dysmorphic features with a history of recurrent sinopulmonary infections. His recurrent pneumonia resulted in a pneumatocele.

DYSMORPHIC FEATURES

- Large forehead
- Down-slanting palpebral features
- Blepharophimosis
- Small nose and ear canals
- Overlapping fingers with camptodactyly of the middle fingers

FIGURES 1 & 2



GENETIC ANALYSIS

- Genetic abnormalities were found using micro array analysis
- Loss of proximal short arm of chromosome 3 (3p12.3 – 3p14.3, 9.35 Mb)

IMMUNOLOGICAL WORK UP

Clinical laboratory investigation at Children's Hospital:
· Low Pneumococcal titers post vaccination
· Reduced T cell proliferation to tetanus antigen

Flow cytometric research analysis at UAB:
· FOXP1 protein reduced in both CD4+ and CD8+ T cells
· IFN-gamma reduced in both CD4+ and CD8+ T cells
· Low numbers of circulating Memory B cells

FIGURE 3

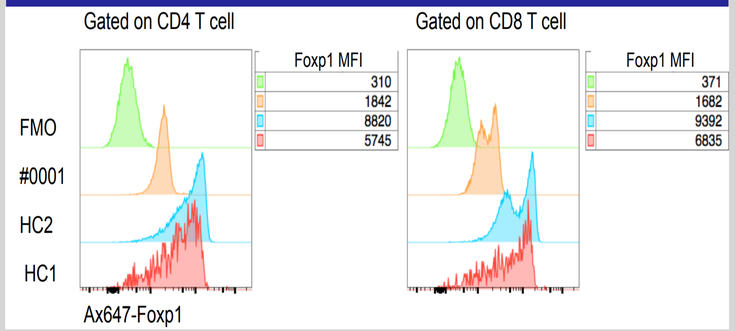


FIGURE 4

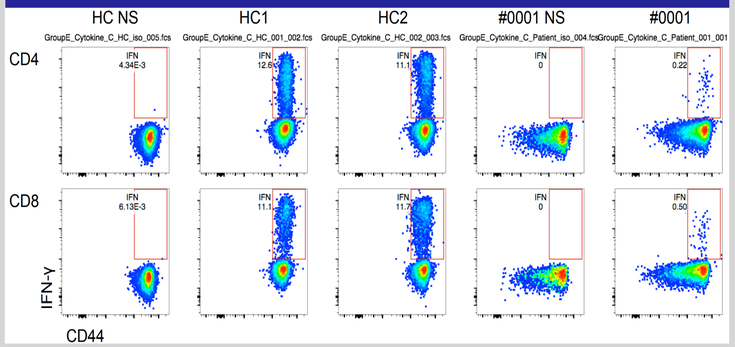
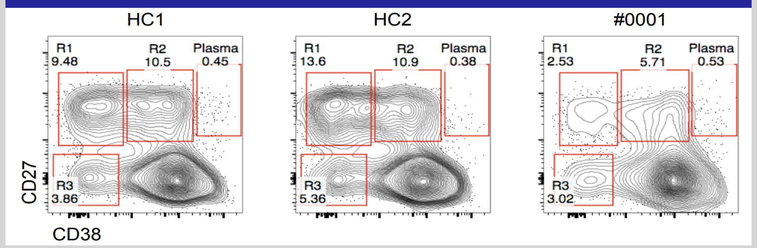


FIGURE 5



PSYCHOLOGICAL EVALUATION

- Autism Spectrum Disorder and Moderate Intellectual Disability (DSM-5)
- Receptive and Expressive language skills as well as functional communication were significantly impaired (Mullen, WASI-II, BASC-3)
- Hyperactivity, Atypicality, and Attention scales were in clinically significant ranges (BASC-3)
- General adaptive, conceptual, social, and practical composite scores were extremely low (ABAS-3)
- Fine motor and visual reception scored in the 1st percentile rank, with age equivalents of 21 and 24 months respectively (Mullen Scale)

FIGURE 6

Mullen Scale	T score	Percentile Rank	Age Equivalent	Classification
Visual Reception – *spatial organization/visual memory*	20	1	24 months	Very Low
Fine Motor – *fine motor dexterity/manipulation of objects*	20	1	21 months	Very Low
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Expressive Language – *the ability to generate language*	20	1	22 months	Very Low

CONCLUSION

- Classic dysmorphic features (overlapping fingers, broad forehead, etc.) and Autism are well-established for patients with FOXP1 deletions.
- This case study found:
  - Low memory B cells
  - Poor pneumococcal vaccine response
  - Low IFN-gamma T cell expression
  - Foxp1 protein expression <50%
  - Psychological evaluation
- These findings implicate Foxp1 as a potential target for future research describing the connection between Autism and the immune system

ACKNOWLEDGMENTS

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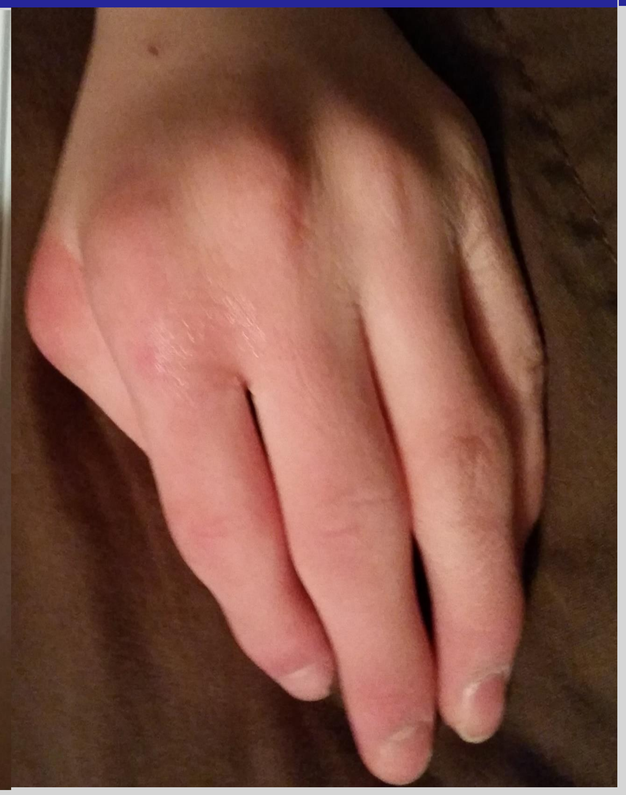

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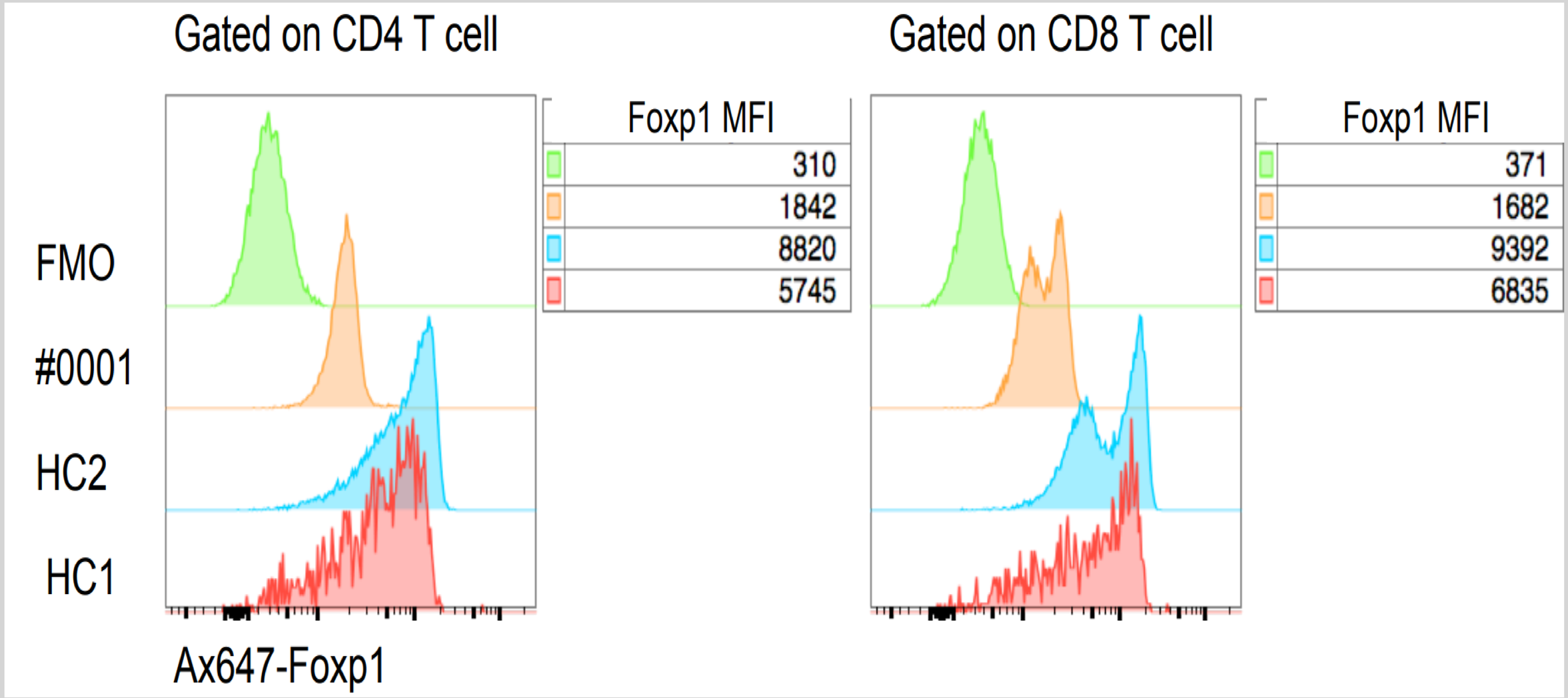
Gated on CD4 T cell
Gated on CD8 T cell
FMO
#0001
HC2
HC1
Foxp1 MFI
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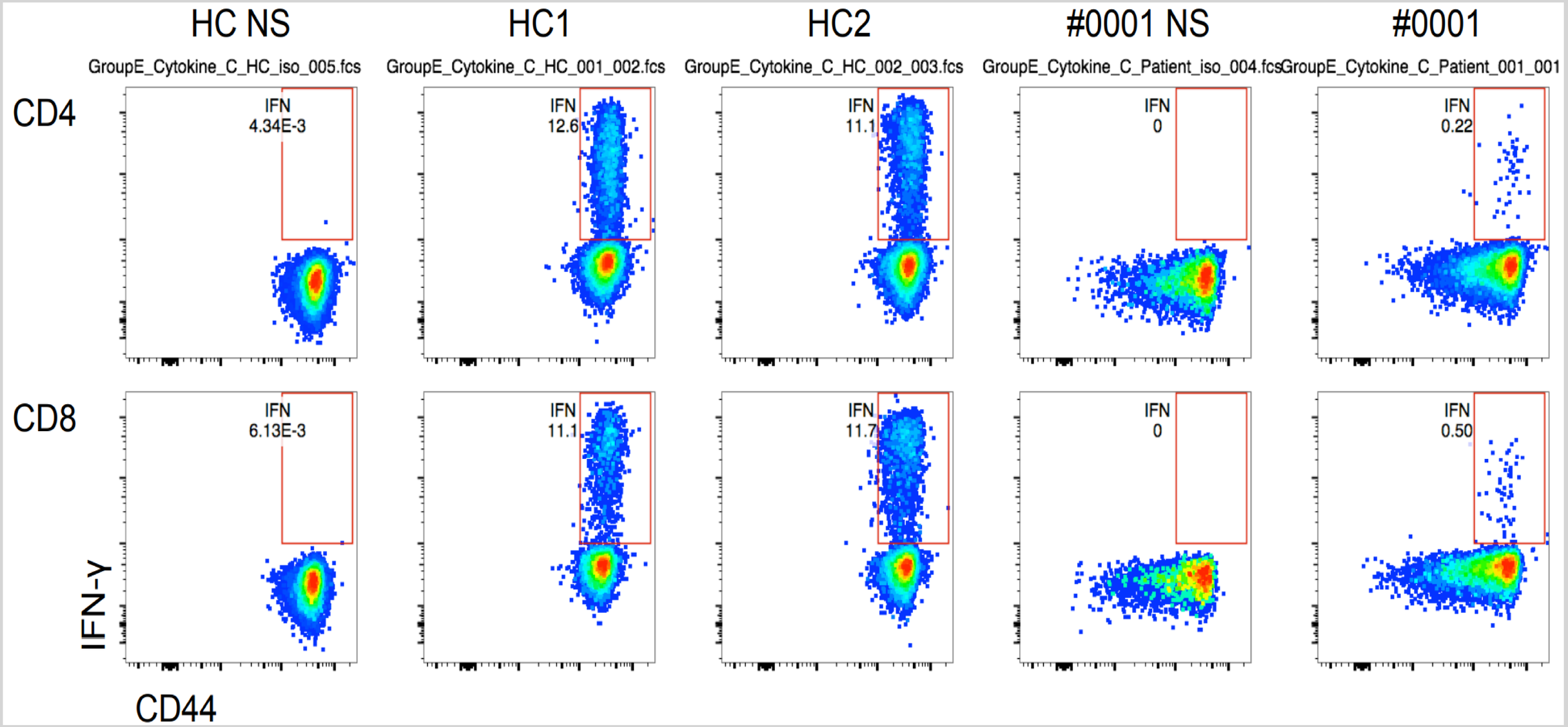
1842
8820
5745
Foxp1 MFI
371
1682
9392
6835
Ax647-Foxp1

FIGURE 4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HC1
HC2
#0001 NS
#0001
GroupE_Cytokine_C_HC_iso_005.fcs
GroupE_Cytokine_C_HC_001_002.fcs
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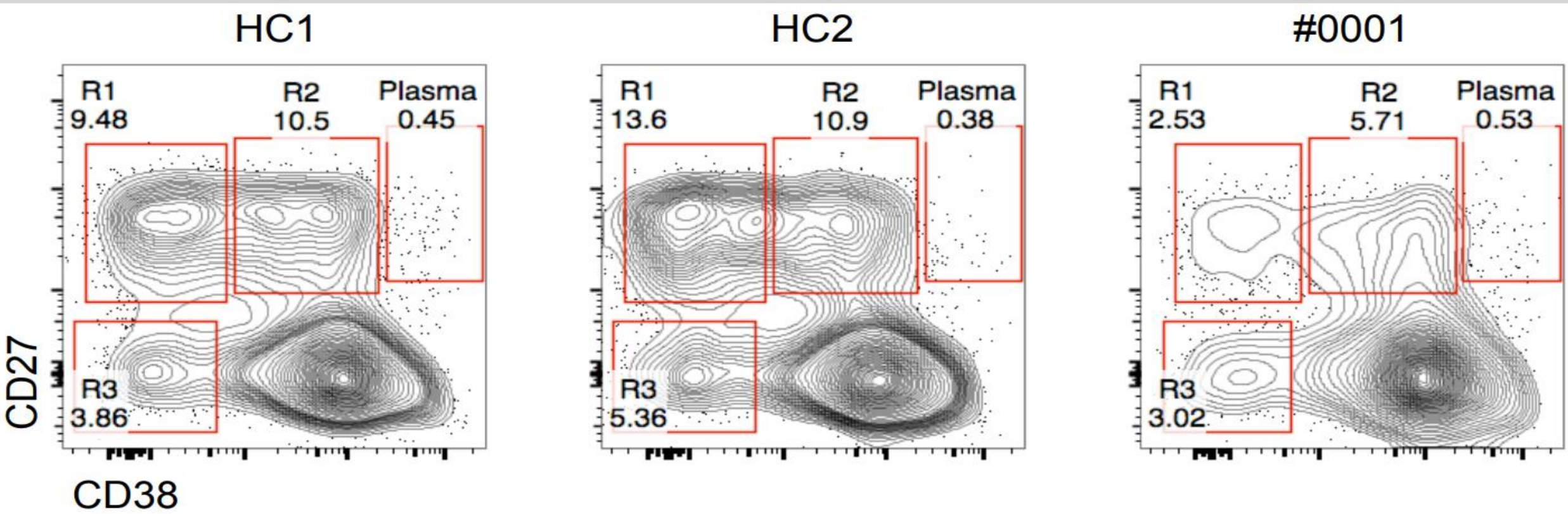
GroupE_Cytokine_C_Patient_iso_004.fcs
GroupE_Cytokine_C_Patient_001_001
CD4
IFN
4.34E-3
IFN
12.6
IFN
11.1
IFN
0
IFN
0.22
CD8
IFN
6.13E-3
IFN
11.1
IFN
11.7
IFN
0
IFN
0.50
IFN-γ
CD44

FIGURE 5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R2
10.5
Plasma
0.45
R3
3.86
HC2
R1
13.6
R2
10.9
Plasma
0.38
R3
5.36
#0001
R1
2.53
R2
5.71
Plasma
0.53
R3
3.02
CD27
CD38

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