Biochemistry, structure, and cellular internalization of a four nanobody-bearing Fc dimer

Eric Chabrol, Charline Fagnen, Sophie Landron, Estelle Marcheteau, Johann Stojko, Sophie-pénélope Guenin, Mathias Antoine, Benjamin Fould, Gilles Ferry, Jean Boutin, et al.

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Stereotactic biopsies of brainstem lesions: dilemma on the best trajectory

Bertrand MATHON, MD[1,2]; Henri MALAIZE, MD[1]; Aymeric AMELOT MD, PhD[1,3].
On behalf of the PSL BRAIN-BIOPSY STUDY GROUP.

1. Department of Neurosurgery, APHP - Sorbonne University, La Pitié-Salpêtrière Hospital, Paris, France.
2. INSERM U 1127, CNRS UMR 7225, Sorbonne University, Paris Brain Institute, ICM, Paris, France.
3. Department of Neurosurgery, Bretonneau Hospital, Tours, France.

Reprints and Correspondence: Bertrand Mathon, MD, MSc, Department of Neurosurgery, La Pitié–Salpêtrière University Hospital, 47–83, boulevard de l'Hôpital, 75651 Paris Cedex 13, France. Tel: +33 (0)1 84 82 73 63; e-mail: bertrand.mathon@aphp.fr

ORCID: 0000-0002-9182-5846

We read with great interest the article by Jaradat et al, entitled "Stereotactic biopsies of brainstem lesions: which approach?" [4]. We commend the authors for sharing their valuable experience on stereotactic biopsies of brainstem lesions. In this retrospective, single-center cohort on 23 adult patients, the authors report a high diagnostic yield (91%) and a low rate of complications (no mortality, 13% of transient neurological morbidity), and discuss the best approach to target brainstem lesions. They recommend a supratentorial transfrontal approach for midbrain lesions, a transcerebellar-transpeduncular route for pontine lesions and for the lesions located in the upper part of the medulla oblongata, and a transfrontal trajectory for the other medullary lesions.

Based on our experience and findings [7, 11], we would like to offer our view and contribution to the field of brainstem biopsies. In a previous study on 1,500 consecutive stereotactic biopsies, we highlighted that brainstem biopsy-targeted lesions was independent predictor of biopsy-related mortality [11]. In the case series from Cheng [3] and Quick-Weller [9], the mortality rates related to brainstem biopsies were also higher than for other targets (2.7% and 3.8%, respectively). As a structure associated with critical functions, biopsies targeting the brainstem may be associated with more functional and even fatal complications [10].

Between April 2009 and October 2020, 50 patients underwent frame-based stereotactic brainstem biopsy at our institution. In this series, 2% of brainstem biopsies were followed by a permanent neurological worsening and 6% of biopsies were fatal. After multivariate analysis, the use of a supratentorial transfrontal approach was the only predictor of post-biopsy symptomatic complications (OR 0.1, 95%CI (0.02-0.9), P = 0.04). In the light of these findings, we suggest using the transcerebellar-transpeduncular trajectory whenever practicable. The transfrontal approach is indicated for midbrain lesions. Concerning the lesions located within the lower part of the medulla oblongata, they can be reached either using a stereotactic transfrontal approach or an infracerebellar open route [12].

Regardless the approach, and more than for any other biopsy target, the number of collected tissue samples must be limited, due to the associated risk of bleeding and neurological injury. Thus, the use of fluorescent agents (e.g., 5-ALA), especially for high-grade glioma[8] and lymphoma [5] patients, may obviate the need for higher numbers of specimens during stereotactic biopsy for diagnosis which may lessen post-biopsy complication rates. In addition, the use of molecular markers [1] and intraoperative diagnostic evaluation using frozen section or smear [6] may also avoid taking too many tissue samples and carrying out a second biopsy in case of initial negativity.

Conflicts of interest

The authors declare no conflicts of interest.

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Ethics and patient consent

As for all observational studies of routinely acquired data, a waiver for written informed consent was obtained.

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A

VHH

IgG1 Fc Domain

Linker

VHH
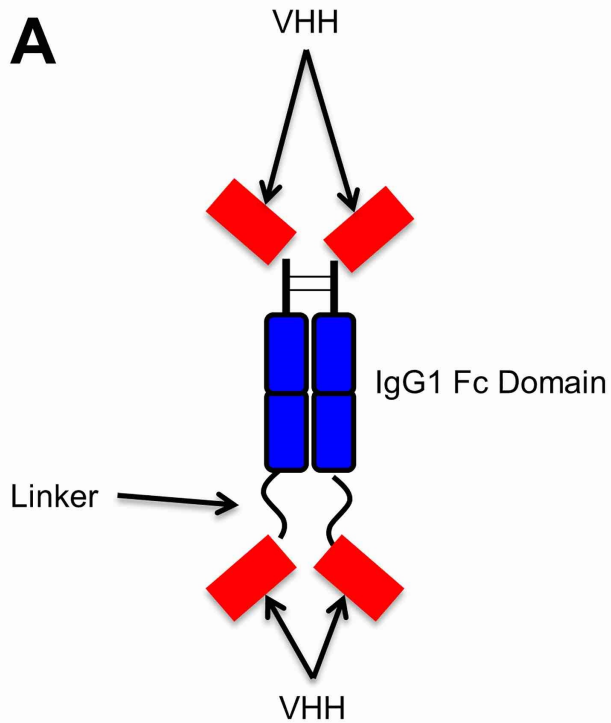
B

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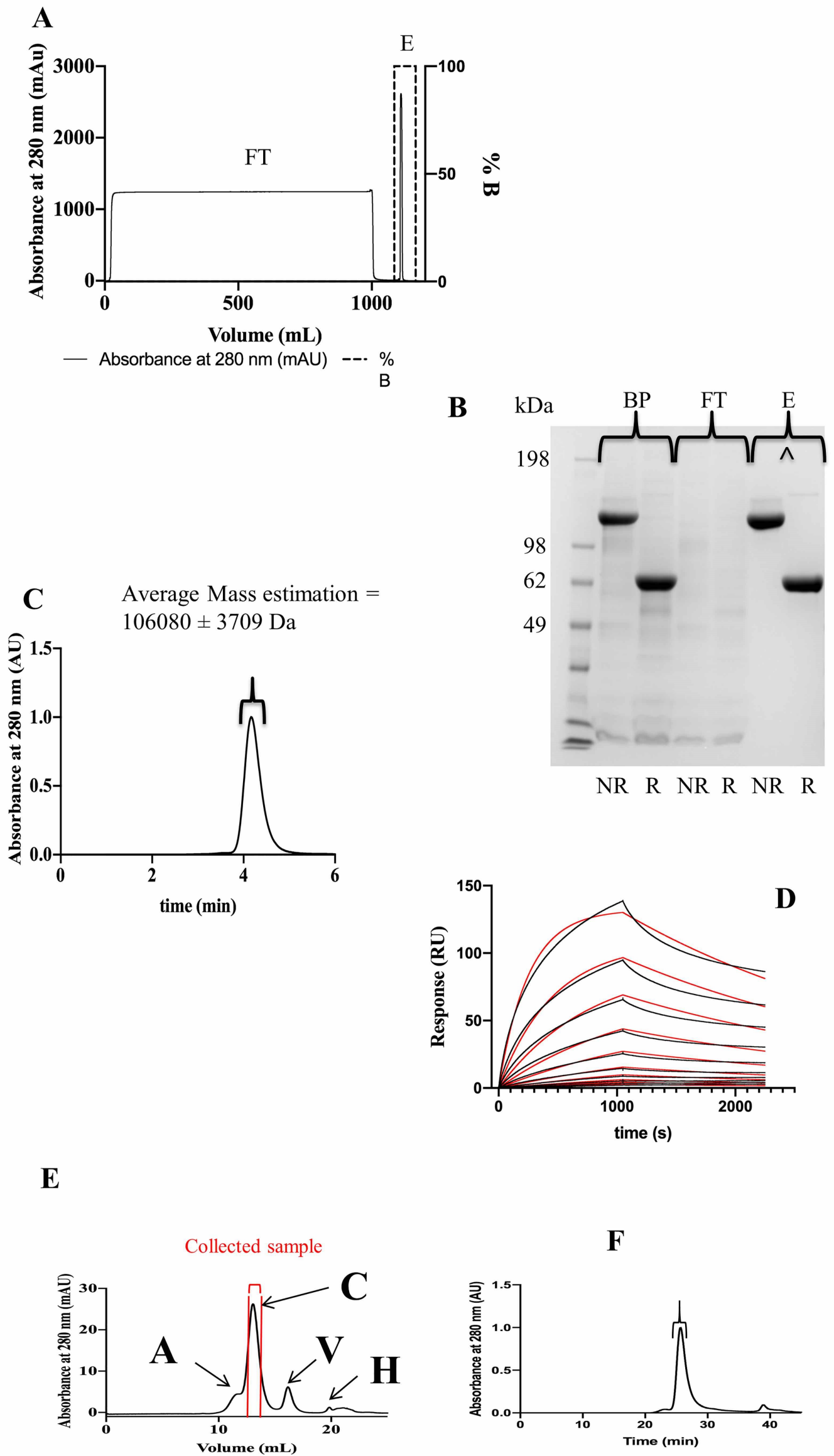KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
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TQKSLSLSPGGGSGGSEVQLVESGGGLVQAGGSLRLS
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ADSVKGRFTISRDNAKNTVYLQMNSLKPEDTAVYYCNA
RWVKPQFIDNNYWGQGTQVTVSS

Figure 1

A

B

C

Average Mass estimation = 106080 ± 3709 Da

D

E

F

Figure 2

52636Da

A deglycosylated

B glycosylated

Δ = 1241 Da (G0 – GlcNac)

+204Da

+162Da

+161Da

G0 (60%)

G1 (28%)

G2 (4%)

(8%)

Figure 3

Figure 4
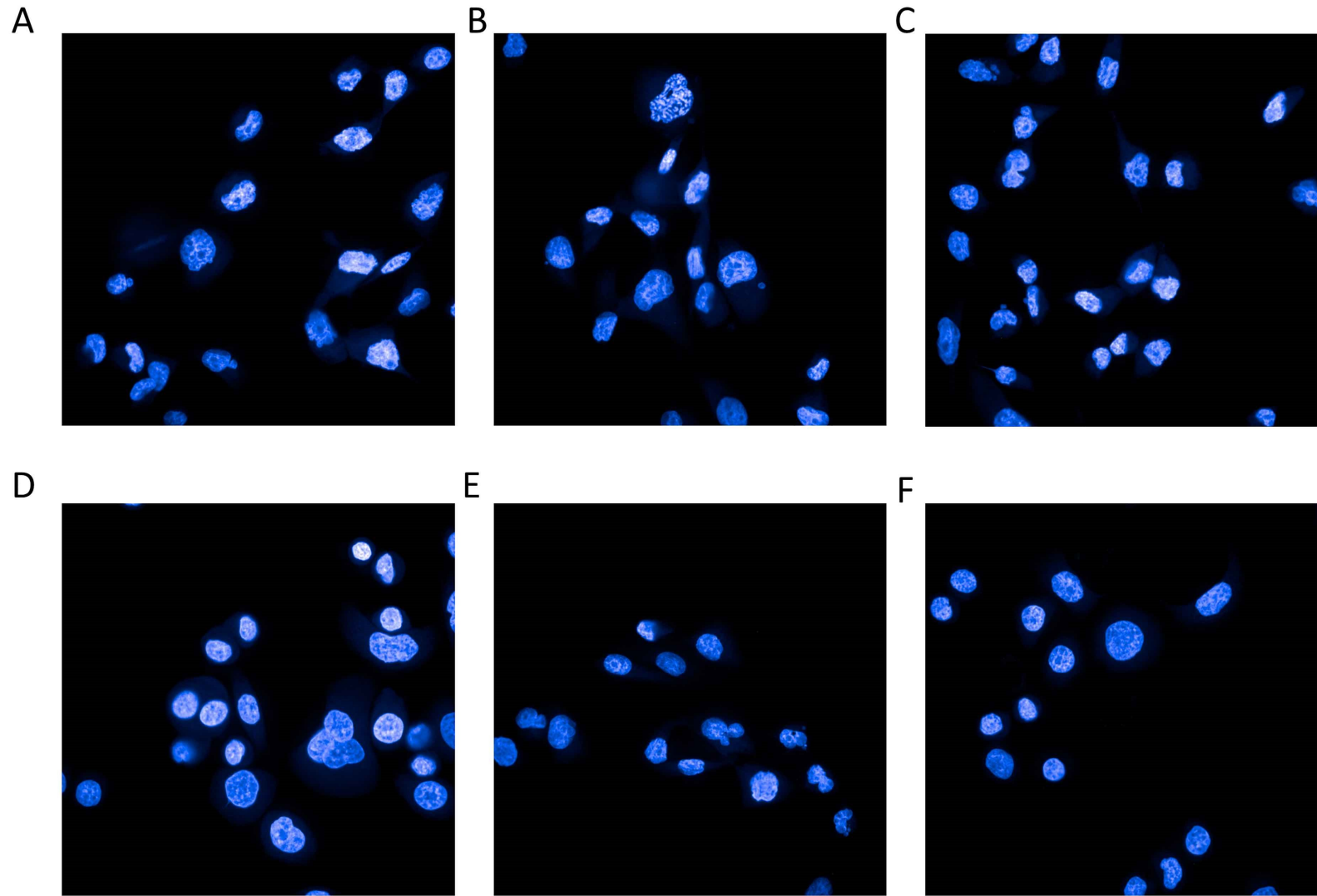
A

B

VHH + HER

IgG
Fc domains

VHH + HER

VHH + HER

C

A B C D E F
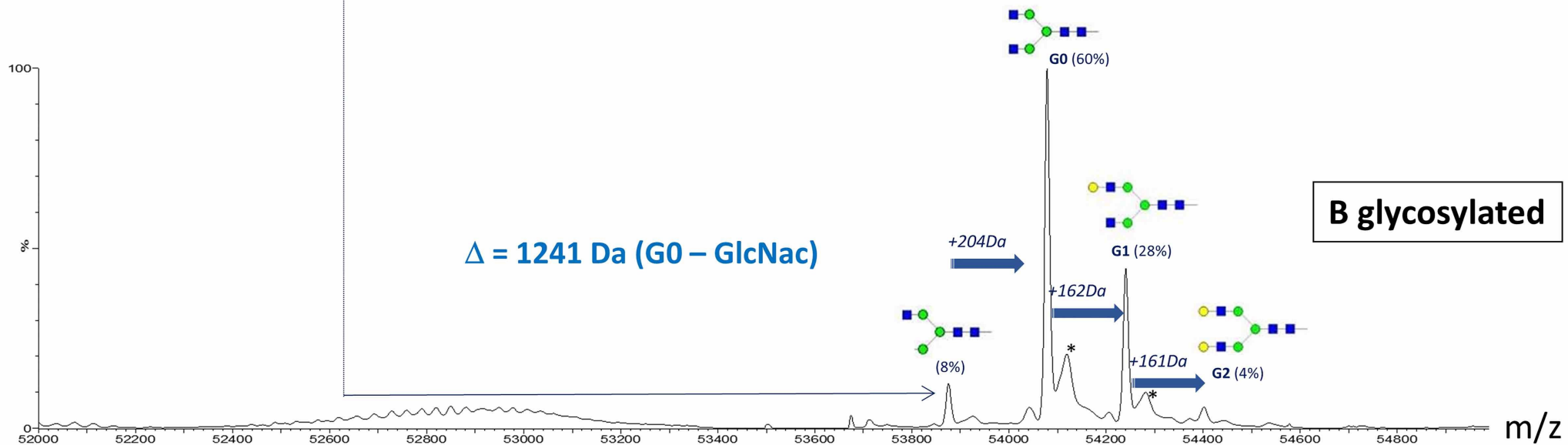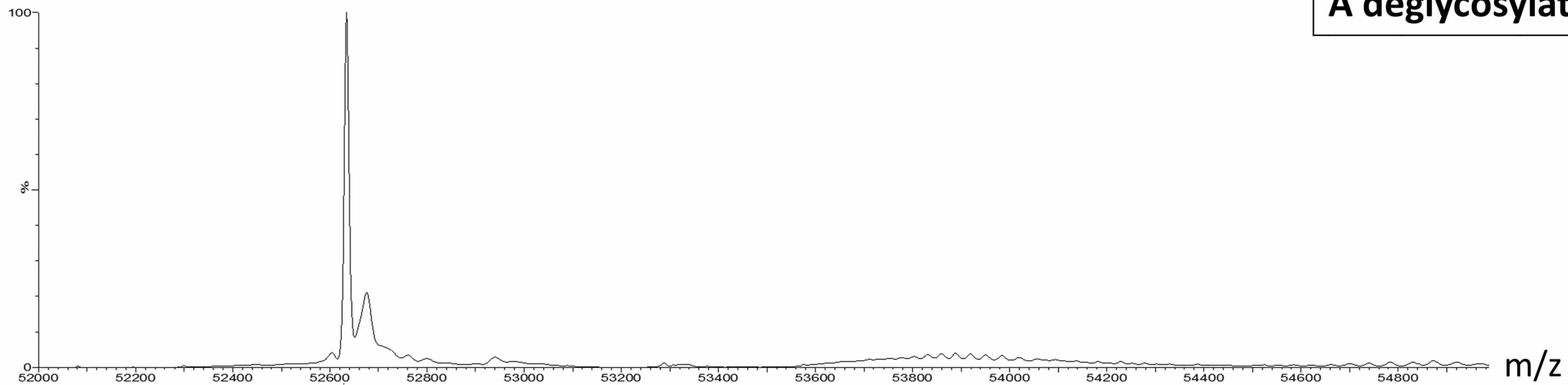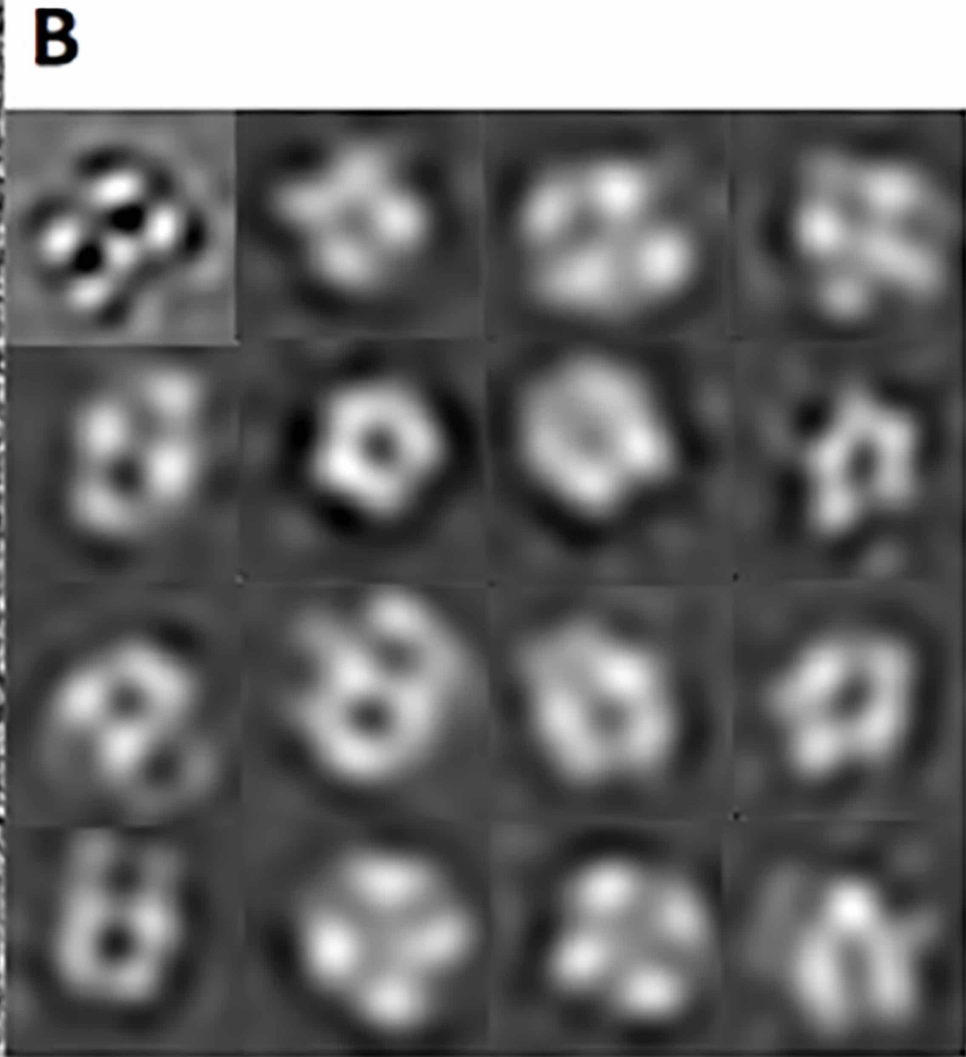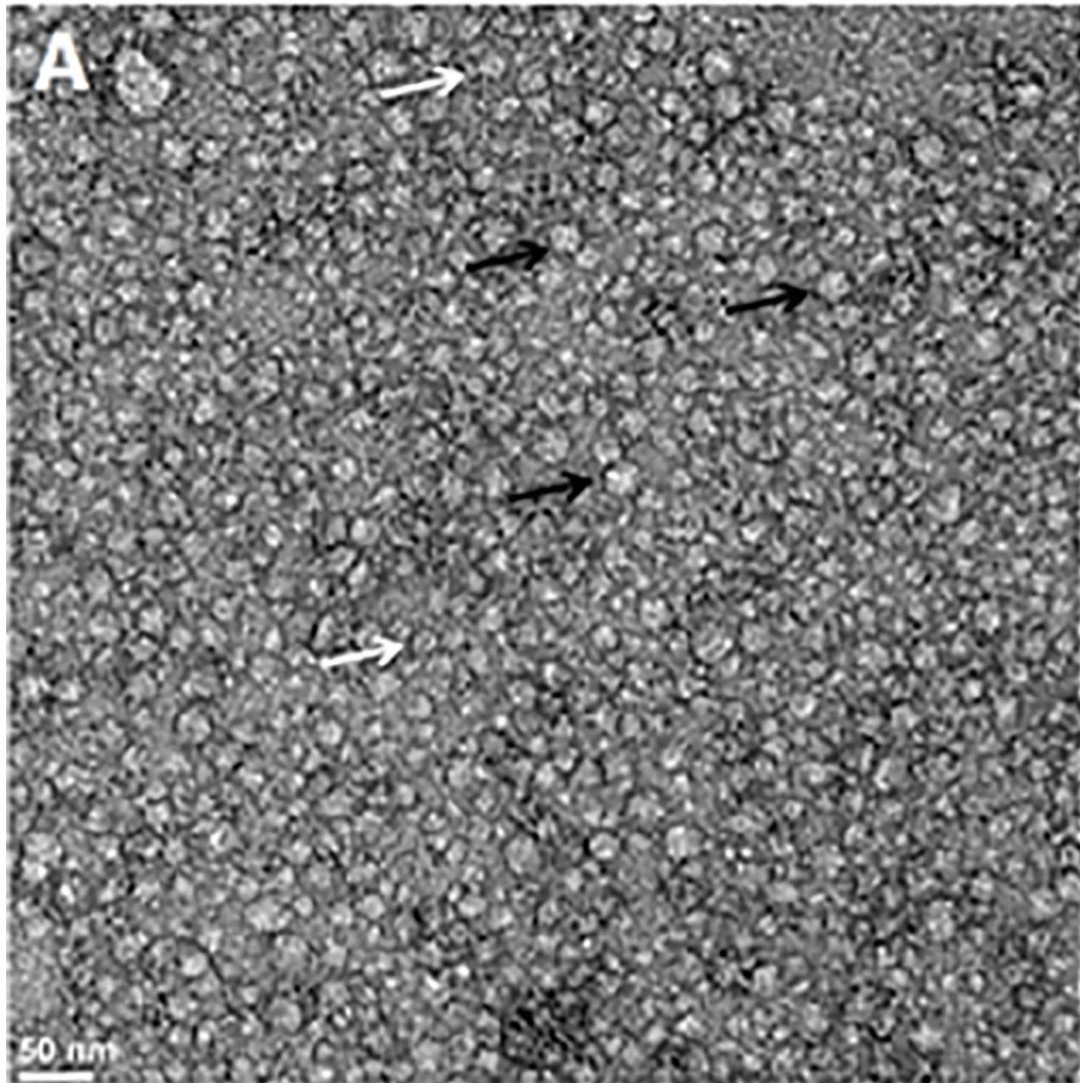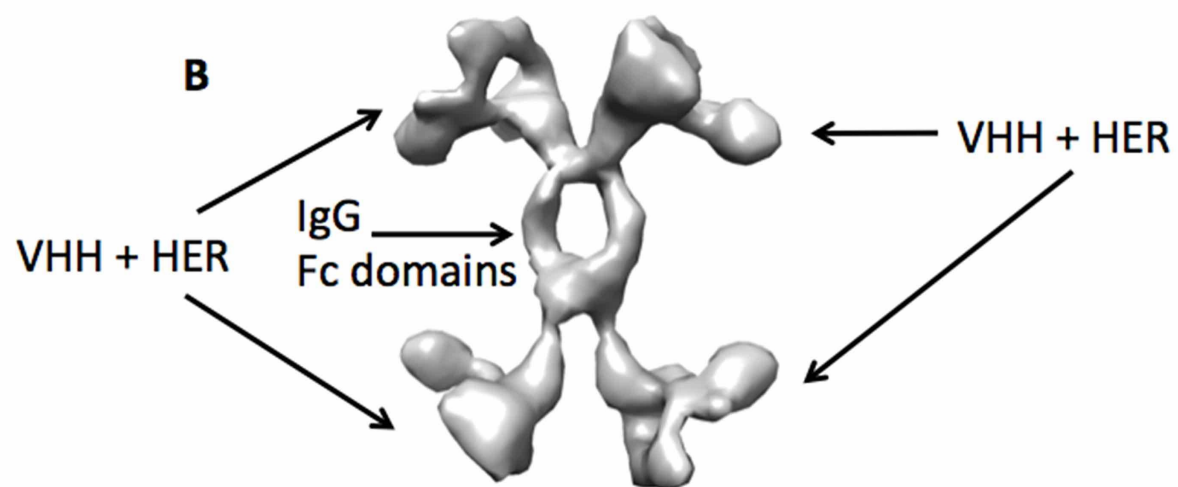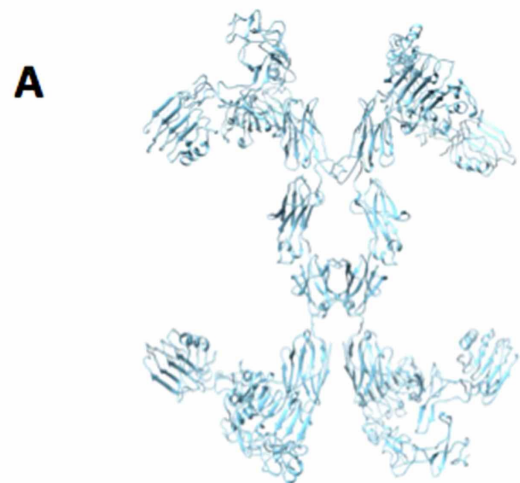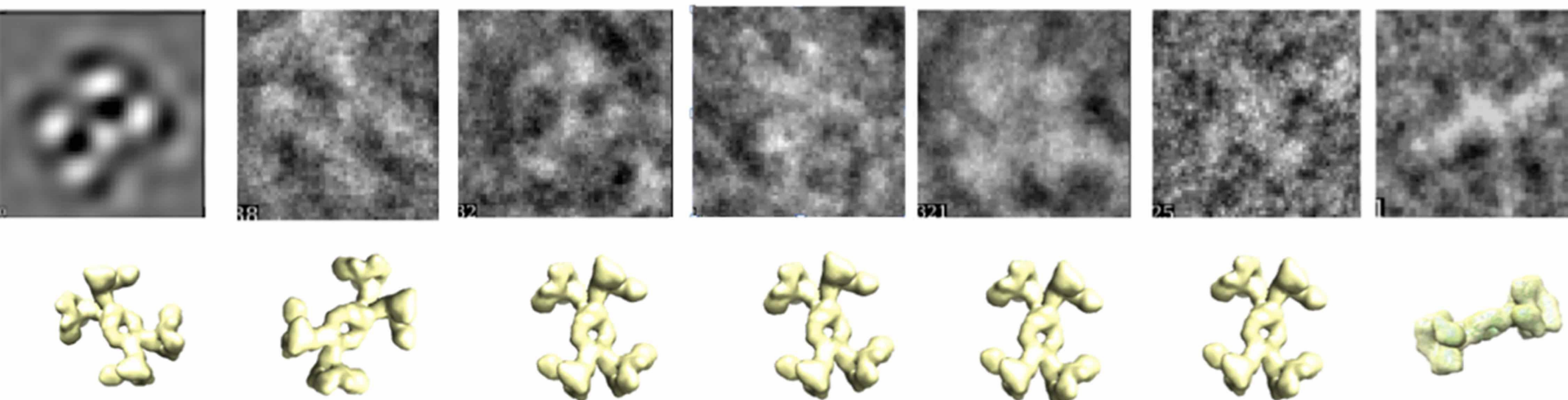
Figure 6

Figure 7

Figure 8