



HAL
open science

Sema4A-Nrp1 versus Sema4A-plexinB2 in the acutely damaged kidney

Amélie Calmont

► **To cite this version:**

Amélie Calmont. Sema4A-Nrp1 versus Sema4A-plexinB2 in the acutely damaged kidney. *Kidney International*, 2022, 101 (2), pp.419. 10.1016/j.kint.2021.10.034 . hal-03542958

HAL Id: hal-03542958

<https://hal.sorbonne-universite.fr/hal-03542958v1>

Submitted on 25 Jan 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Sema4A-Nrp1 versus Sema4A-PlexinB2 in the acutely damaged kidney

Journal:	<i>Kidney International</i>
Manuscript ID	KI-10-21-1724
Article Type:	Letter to the Editor
Date Submitted by the Author:	06-Oct-2021
Complete List of Authors:	Calmont, Amelie; inserm UMR S1155,
Keywords:	acute kidney injury, ischemia reperfusion, signaling
Subject Area:	Acute Kidney Injury

SCHOLARONE™
Manuscripts

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Arbitrary title:

Sema4A-Nrp1 versus Sema4A-PlexinB2 in the acutely damaged kidney

Amélie Calmont¹

¹ INSERM UMRS 1155, Kidney Research Centre, Tenon Hospital, 4 rue de la Chine, 75020 Paris, France. amelie.calmont@inserm.fr
Phone: +33156018375

Refers to:

The semaphorin 4A–neuropilin 1 axis alleviates kidney ischemia reperfusion injury by promoting the stability and function of regulatory T cells.

Junnan Xu, Xiubin Li, Qing Yuan, Chenfeng Wang, Liang Xu, Xing Wei, Haitao Liu, Bo Yu, Zhekun An, Yuanyu Zhao, Xiang Li, Xu Zhang, Xin Ma, Ming Cai
September 14, 2021 DOI: <https://doi.org/10.1016/j.kint.2021.08.023>

1
2
3
4 We read with great interest the article by Xu et al. recently published in Kidney International¹. This
5
6 study reported that Sema4A systemic delivery could help recruit Neuropilin-1 (Nrp1)- positive
7
8 regulatory T cells (Tregs) to the kidney and alleviate Ischemia Reperfusion Injury (IRI). These
9
10 encouraging results need to be reconciled with previous studies by Xia and colleagues² who
11
12 investigated the respective contribution to IRI of Semaphorins and their receptors Plexins³. These
13
14 authors did not find changes in either kidney function or kidney damage in PlexinB2-deficient mice
15
16 48 hours post IRI. Furthermore they could not detect renal defects in Sema4A-, Sema4B-, Sema4C-
17
18 , Sema4D-, and Sema4G-deficient mice 7 days post injury. Solely the analysis of triple-knockout
19
20 mice lacking Sema4B/Sema4D/Sema4G uncovered a role for the class-4 Semaphorin family in
21
22 kidney repair. While this work emphasised the level of redundancy among these proteins, it also
23
24 undermined the potential role played by Sema4A alone in the development of IRI.
25
26
27
28

29 Another point that deserves special attention is the potential role of circulating Sema4A. Class-4
30
31 semaphorins including Sema4A⁴ can be released from the cell membrane by proteolytic cleavage
32
33 and be secreted, then using Neuropilins as their receptors and Plexins as co-receptors³. Whether
34
35 secreted Sema4A could help recruit Nrp1-positive Tregs to the damaged kidney is a possibility,
36
37 although questionable. Indeed, no increase in Sema4A serum concentration in mice following IRI
38
39 (supplemental Fig10) and in patients who underwent partial nephrectomy (Supplemental Fig13)
40
41 were reported by Xu *et al.*¹.
42
43
44

45 Overall, Xu and colleagues described a rather efficient, albeit artificial, way to overcome IRI and
46
47 provided convincing data for the implication of the Sema4A-Nrp1 axis. However, their findings are
48
49 to be pondered in the physiological context of AKI where Sema4a is likely to have no effect in IRI
50
51 development.
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1. Xu J, Li X, Yuan Q, et al. The semaphorin 4A–neuropilin 1 axis alleviates kidney ischemia reperfusion injury by promoting the stability and function of regulatory T cells. *Kidney International*. 2021/09/14/2021;doi:<https://doi.org/10.1016/j.kint.2021.08.023>
2. Xia J, Swiercz JM, Banon-Rodriguez I, et al. Semaphorin-Plexin Signaling Controls Mitotic Spindle Orientation during Epithelial Morphogenesis and Repair. *Dev Cell*. May 4 2015;33(3):299-313. doi:10.1016/j.devcel.2015.02.001
3. Adams RH, Eichmann A. Axon guidance molecules in vascular patterning. *Cold Spring Harbor perspectives in biology*. May 2010;2(5):a001875. doi:10.1101/cshperspect.a001875
4. Carneiro T, Affandi AJ, Malvar-Fernández B, et al. Induction of Inflammation and Fibrosis by Semaphorin 4A in Systemic Sclerosis. *Arthritis & rheumatology (Hoboken, NJ)*. Oct 2019;71(10):1711-1722. doi:10.1002/art.40915

For Peer Review Only