Benefits and limits of decellularization on mass-spectrometry-based extracellular matrix proteome analysis of mouse kidney

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Abstract

Extracellular matrix (ECM) proteins, including collagens, ECM glycoproteins, and proteoglycans, are critical components of tissue structure and function. In addition to the core matrisome, there are matrisome-associated proteins that balance ECM production and degradation. The identification and quantification of ECM proteins using mass spectrometry is often hindered by their low abundance and their tendency to aggregate, forming insoluble macromolecules in aqueous solutions. In this study, we aimed to investigate the effectiveness of a decellularization strategy that combined freeze-thaw cycles and sodium dodecyl sulphate treatment, in identifying and quantifying ECM proteins in mouse kidney using mass spectrometry. This decellularization strategy preserved 95% of the Core matrisome proteins detected in non-decellularized kidney and revealed additional once. Decellularization also led to an increase in the abundance of 96% of the core matrisome ECM proteins by an average of 59 times due to the successful removal of cellular and matrisome-associated proteins. However, the enrichment varied greatly among ECM proteins, resulting in a misrepresentation of the native ECM protein composition of the kidney. This should be brought to the attention of the matrisome research community, as it highlights the need for caution when interpreting proteomic data obtained following a decellularization procedure.

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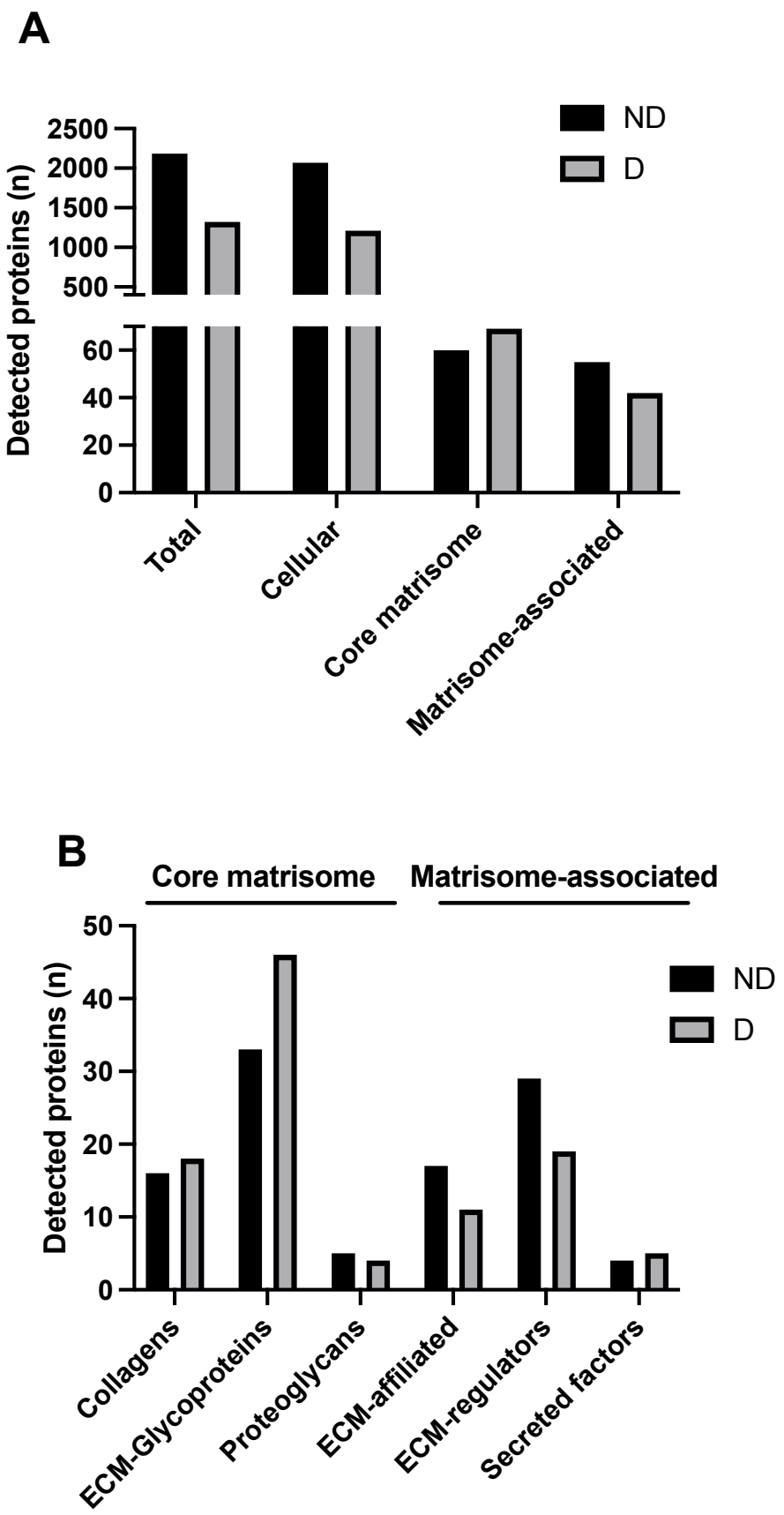

A
ND
D
Detected proteins (n)
2500
2000
1500
1000
500
60
40
20
0
Total
Cellular
Core matrisome
Matrisome-associated
B
Core matrisome
Matrisome-associated
ND
D
Detected proteins (n)
50
40
30
20
10
0
Collagens
ECM-Glycoproteins
Proteoglycans
ECM-affiliated
ECM-regulators
Secreted factors

Figure 1

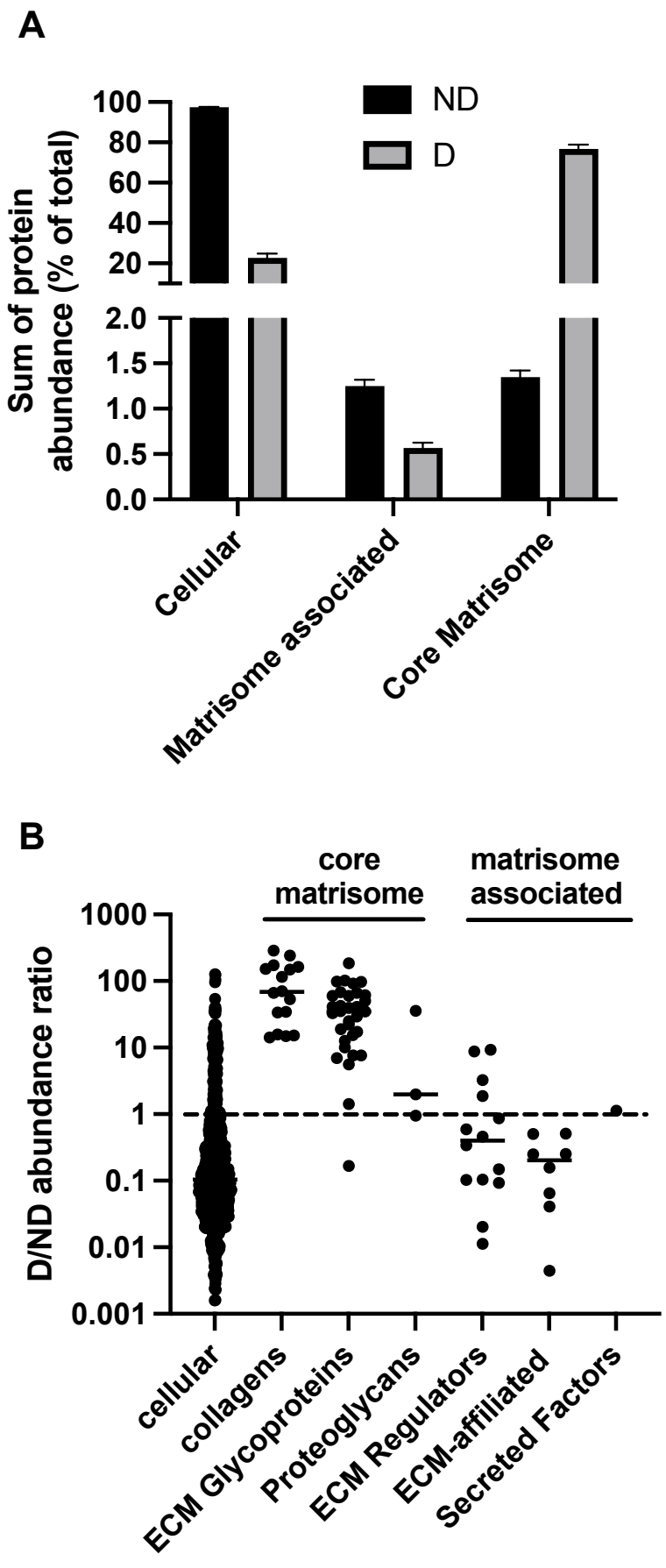
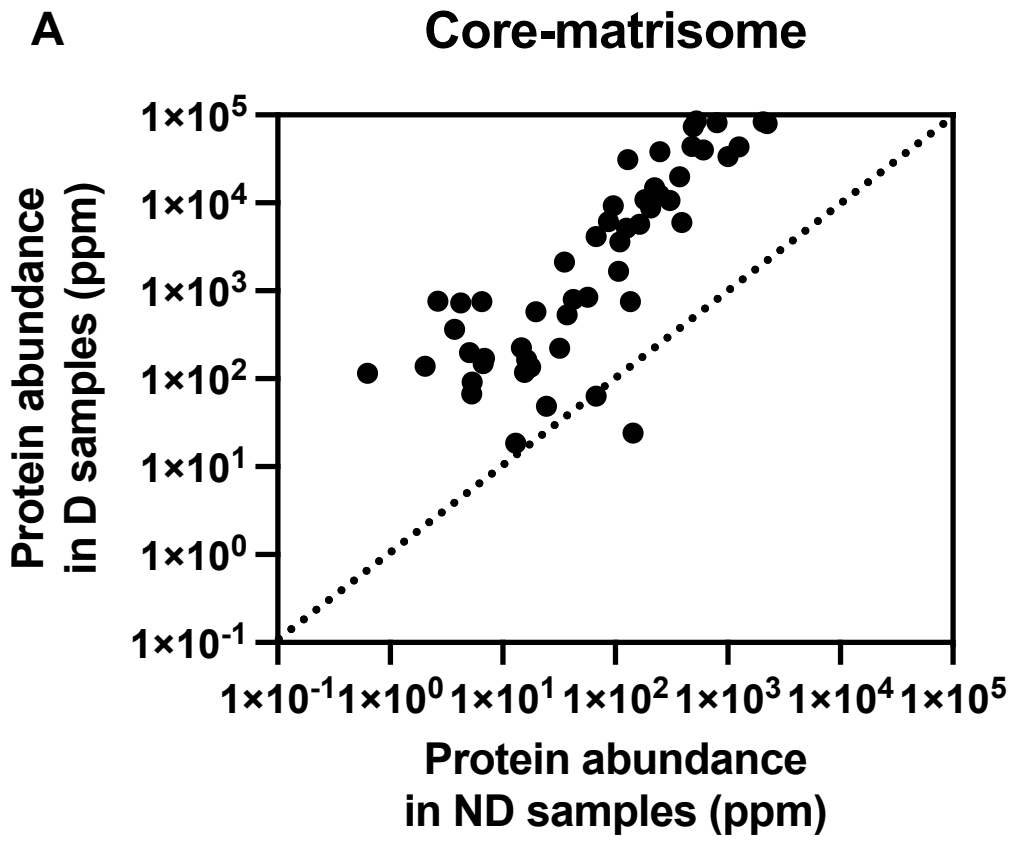

A
ND
D
Sum of protein abundance (% of total)
100
80
60
40
20
2.0
1.5
1.0
0.5
0.0
Cellular
Matrisome associated
Core Matrisome
B
core matrisome
matrisome associated
D/ND abundance ratio
1000
100
10
1
0.1
0.01
0.001
cellular
collagens
ECM Glycoproteins
Proteoglycans
ECM Regulators
ECM-affiliated
Secreted Factors

Figure 2


A
Core-matrisome
Protein abundance in D samples (ppm)
1×10^5
1×10^4
1×10^3
1×10^2
1×10^1
1×10^0
1×10^-1
1×10^-1 1×10^0 1×10^1 1×10^2 1×10^3 1×10^4 1×10^5
Protein abundance in ND samples (ppm)

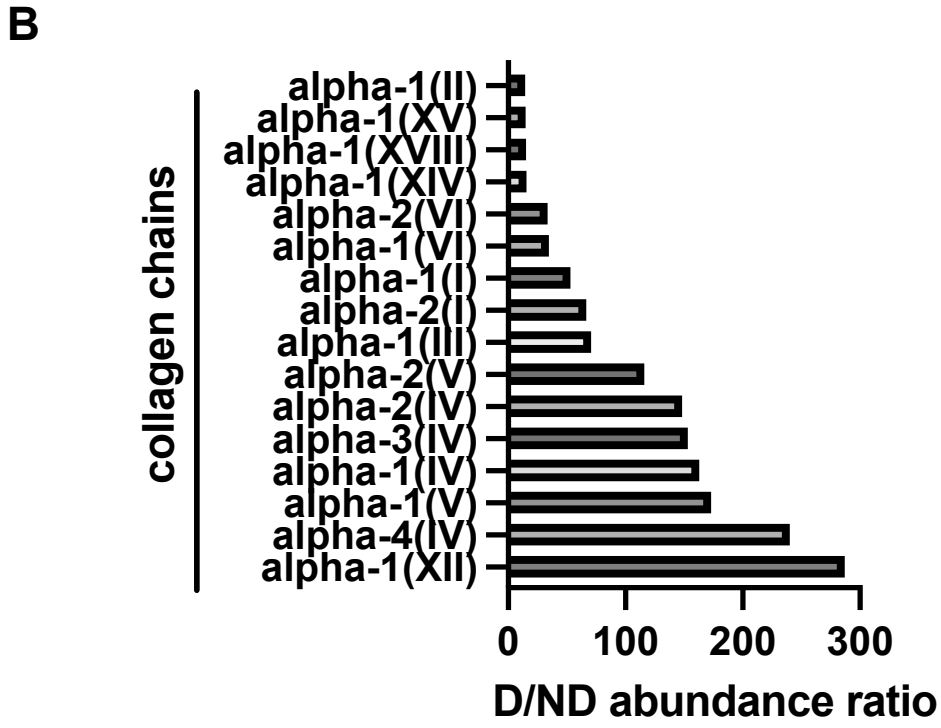

B
collagen chains
alpha-1(II)
alpha-1(XV)
alpha-1(XVIII)
alpha-1(XIV)
alpha-2(VI)
alpha-1(VI)
alpha-1(I)
alpha-2(I)
alpha-1(III)
alpha-2(V)
alpha-2(IV)
alpha-3(IV)
alpha-1(IV)
alpha-1(V)
alpha-4(IV)
alpha-1(XII)
0
100
200
300
D/ND abundance ratio

Figure 3