Supporting Information for:

Advances in Optical Sensors of N-acetyl-β-D-Hexosaminidase (N-acetyl-β-D-Glucosaminidase)

Janeala J. Morsby and Bradley D. Smith*
Department of Chemistry and Biochemistry
251 Nieuwland Science Hall
University of Notre Dame,
IN 46556-5670, USA
*smith.115@nd.edu

Table S1. List of average changes in urinary HEX(NAG) levels that have been reported in the literature for a range of different clinical conditions.

Disease or Condition	Number of Patients	Approximate Ratio of Human Urinary HEX(NAG) Level Over Normal Condition	Reference
Type II Diabetes	592	~2	1
	57	~5	2
	80	~2	3
	160	~1.1	4
	800	~10	5
	50	~ 6	6
Type 1 Diabetes	215	2.4	7
	25	~1.8	8
	204	~2	9
Acute Kidney Injury	402	~3.4	10
	135	~1.5	11
Chronic Kidney Disease	80	~1.5	12
Polycystic Kidney Disease	270	~2	13
Vesicoureteric Reflux	115	~3.5	14
Urolithiasis	81	~2.6	15
Diabetic Nephropathy	149	~12.6	16
COVID-19	18	~6	17
Acute Renal Failure	201	~3	18
Cisplatin Treated Cancer patients	30	~1.4	19
Contrast Induced Nephropathy	33	~2	20
Asthmatic Children	73	~7.6	21
Antibiotic Treatment for Cystic Fibrosis	88	~3.5	22
Percutaneous Nephrolithotripsy	90	~3.4	23

Notes:

1. Virtually all the literature on urinary N-acetyl-β-D-Glucosaminidase uses a term like NAG, although this table uses the term HEX(NAG).
2. This table reports the average ratio for urinary HEX(NAG) levels in a cohort of patients with a common condition divided by the levels in a related control group of healthy patients. Unambiguous comparison between the different studies is not possible; in large part, because the studies often report different units for the urinary HEX(NAG) levels.

References:

(1) Kim, S. R.; Lee, Y. -H.; Lee, S. -G.; Kange. S.; Cha, B. - S.; Kim, J. -H.; Lee, B. -W. Urinary N-Acetyl-β-D-Glucosaminidase, an Early Marker of Diabetic Kidney Disease, Might Reflect Glucose Excursion in Patients with Type 2 Diabetes. *Medicine* **2016**, *95* (27), 4114. https://journals.lww.com/md-journal/Fulltext/2016/07050/Urinary_N_acetyl___D_glucosaminidase,_an_early.59.aspx

(2) Mohammadi-Karakani, A.; Asgharzadeh-Haghighi, S.; Ghazi-Khansari, M.; Hosseini, R. Determination of Urinary Enzymes as a Marker of Early Renal Damage in Diabetic Patients. *J. Clin. Lab. Anal.* **2007**, *21* (6), 413–417. https://doi.org/10.1002/jcla.20212.

(3) Basturk, T.; Altuntaş, Y.; Kurklu, A.; Aydin, L.; Eren, N.; Unsal, A. Urinary N-Acetyl-β-Glucosaminidase as an Earlier Marker of Diabetic Nephropathy and Influence of Low-Dose Perindopril/Indapamide Combination. *Ren. Fail.* **2006**, *28* (2), 125–128. https://doi.org/10.1080/08860220500530510.

(4) Kopf, S.; Oikonomou, D.; Zdunek, D.; von Eynatten, M.; Hess, G.; Nawroth, P. P.; Bierhaus, A.; Humpert, P. M. Urinary N-Acetyl-Beta-D-Glucosaminidase Excretion: An Indicator of Neuropathy in Type 2 Diabetes. *Exp Clin Endocrinol Diabetes* **2013**, *121* (10), 601–606. https://doi.org/10.1055/s-0033-1355384.

(5) Pocsi, I.; Taylor, S. A.; Richardson, A. C.; Aamlid, K. H.; Smith, B. V.; Price, R. G. "VRA-GlcNAc": Novel Substrate for N-Acetyl-β-D-Glucosaminidase Applied to Assay of This Enzyme in Urine. *Clin. Chem.* **1990**, *36* (11), 1884–1888. https://doi.org/10.1093/clinchem/36.11.1884.

(6) Shibata, H.; Yagi, T. Rate Assay of N-Acetyl-B-D-Hexosaminidase with 4-Nitrophenyl N-Acetyl-β-D-Glucosaminidase as an Artificial Substrate. *Clin. Chim. Acta* **1996**, *251* (1), 53–64. https://doi.org/10.1016/0009-8981(96)06292-4.

(7) Kordonouri, O.; Jörres, A.; Müller, C.; Enders, I.; Gahl, G. M.; Weber, B. Quantitative Assessment of Urinary Protein and Enzyme Excretion - a Diagnostic Programme for the Detection of Renal Involvement in Type I Diabetes Mellitus. *Scand. J. Clin. Lab. Invest.* **1992**, *52* (8), 781–790. https://doi.org/10.3109/00365519209088381.

(8) Omozee, E. B.; Okaka, E. I.; Edo, A. E. Urinary N-Acetyl-β-D-Glucosaminidase Levels in Diabetic Adults. *J. Lab. Physicians* **2020**, *11* (1), 1–4. https://doi.org/10.4103/JLP.JLP.

(9) Hong, N.; Lee, M.; Park, S.; Lee, Y. H.; Jin, S. M.; Kim, J. H.; Lee, B. W. Elevated Urinary N-Acetyl-β-D-Glucosaminidase Is Associated with High Glycoalbumin-To-Hemoglobin A1c Ratio in Type 1 Diabetes Patients with Early Diabetic Kidney Disease. *Sci. Rep.* **2018**, *8* (1), 6710–6718. https://doi.org/10.1038/s41598-018-25023-5.

(10) Kaufmann, M.; Schlossbauer, M.; Hubauer, U.; Stadler, S.; Fischer, M.; Wallner, S.; Hupf, J.; Zimmermann, M.; Orso, E.; Zeman, F.; Luchner, A.; Maier, L.; Jungbauer, C. N-Acety-β-D-Glucosaminidase: A Potential Biomarker for Early Detection of Acute Kidney Injury in Acute Chest Pain. *Nephrology* **2020**, *25* (2), 135–143. https://doi.org/10.1111/nep.13664.

(11) Fan, H.; Zhao, Y.; Sun, M.; Zhu, J. H. Urinary Neutrophil Gelatinase-Associated Lipocalin, Kidney Injury Molecule-1, N-Acetyl-β-D-Glucosaminidase Levels and Mortality Risk in Septic Patients with Acute Kidney Injury. *Arch. Med. Sci.* **2018**, *14* (6), 1381–1386. https://doi.org/10.5114/aoms.2018.79006.

(12) Carter.J.L., Parker. C.T, Stevens, P., Eaglestone, G., Knight, S., Farmer, C., Lamb, E. J. Biological Variation of Plasma and Urinary Markers of Acute Kidney Injury in Patients with Chronic Kidney Disease. *Gen. Clin. Chem.* **2016**, *62* (6), 876–883. https://academic.oup.com/clinchem/article/62/6/876/5611874?login=true

(13) Park, H. C.; Hwang, J. H.; Kang, A. -Y.; Ro, H.; Kim, M. G.; An, J. N.; Park, J. I.; Kim, S. H.; Yang, J.; Oh, Y. K.; Oh, K. -H.; Noh, J. W.; Cheong, H. I.; Hwang, Y. -H.; Ahn, C. Urinary N-Acetyl D-Glucosaminidase as a Surrogate Marker for Renal Function in Autosomal Dominant Polycystic Kidney Disease: 1 Year Prospective Cohort Study. *BMC Nephrol.* **2012**, *13* (1), 1–10. https://doi.org/10.1186/1471-2369-13-93.

(14) Miyakita, H.; Puri, P. Urinary Levels of N-Acetyl-Beta-D-Glucosaminidase: A Simple Marker for Predicting Tubular Damage in Higher Grades of Vesicoureteric Reflux. *Eur. Urol.* **1994**, *25* (2), 135–137. https://doi.org/10.1159/000475267.

(15) Balla, A. A.; Salah, A. M.; Abdalmotaal, E.; Hoppe, B.; Bongartz, D.; Kessler, T.; Hesse, A. N-Acetyl-β-D-Glucosaminidase Excretion in Healthy Children and in Pediatric Patients with Urolithiasis. *World J. Urol.* **1998**, *16* (6), 413–416. https://link.springer.com/article/10.1007%2Fs003450050093

(16) Mise, K.; Hoshino, J.; Ueno, T.; Hazue, R.; Hasegawa, J.; Sekine, A.; Sumida, K.; Hiramatsu, R.;

Hasegawa, E.; Yamanouchi, M.; Hayami, N.; Suwabe, T.; Sawa, N.; Fujii, T.; Hara, S.; Ohashi, K.; Takaichi, K.; Ubara, Y. Prognostic Value of Tubulointerstitial Lesions, Urinary N-Acetyl-β-D-Glucosaminidase, and Urinary B2-Microglobulin in Patients with Type 2 Diabetes and Biopsy–Proven Diabetic Nephropathy. *Clin. J. Am. Soc. Nephrol.* **2016**, *11* (4), 593–601. https://doi.org/10.2215/CJN.04980515.

(17) Fukao, Y.; Nagasawa, H.; Nihei, Y.; Hiki, M.; Naito, T.; Kihara, M.; Gohda, T.; Ueda, S.; Suzuki, Y. COVID-19-Induced Acute Renal Tubular Injury Associated with Elevation of Serum Inflammatory Cytokine. *Clin. Exp. Nephrol.* **2021**, *25* (11), 1240–1246. https://doi.org/10.1007/s10157-021-02101-z.

(18) Liangos, O.; Perianayagam, M. C.; Vaidya, V. S.; Han, W. K.; Wald, R.; Tighiouart, H.; MacKinnon, R. W.; Li, L.; Balakrishnan, V. S.; Pereira, B. J. G.; Bonventre, J. V.; Jaber, B. L. Urinary N-Acetyl-β-(D)-Glucosaminidase Activity and Kidney Injury Molecule-1 Level Are Associated with Adverse Outcomes in Acute Renal Failure. *J. Am. Soc. Nephrol.* **2007**, *18* (3), 904–912. https://doi.org/10.1681/ASN.2006030221.

(19) Sakalli, H.; Calikusu, Z.; Sariakcali, B.; Polat, A.; Canatarogu, A. Urinary N-Acetyl-Beta-D-Glucosaminidase Levels In Cancer Patients Treated With Cisplatin. *Nobel Med.* **2013**, *9* (1), 56–60. https://www.nobelmedicus.com/en/Article.aspx?m=380.

(20) Ren, L.; Ji, J.; Fang, Y.; Jiang, S. H.; Lin, Y. M.; Bo, J.; Qian, J. Y.; Xu, X. H.; Ding, X. Q. Assessment of Urinary N-Acetyl-β-Glucosaminidase as an Early Marker of Contrast-Induced Nephropathy. *J. Int. Med. Res.* **2011**, *39* (2), 647–653. https://doi.org/10.1177/147323001103900234.

(21) Demir, A. D.; Goknar, N.; Oktem, F.; Özkaya, E.; Yazıcı, M.; Torun, E.; Vehapoğlu, A.; Kucukkoc, M. Renal Tubular Function and Urinary N-Acetyl-β-D-Glucosaminidase and Kidney Injury Molecule-1 Levels in Asthmatic Children. *Int. J. Immunopathol. Pharmacol.* **2016**, *29* (4), 626–631. https://doi.org/10.1177/0394632016651448.

(22) Etherington, C.; Bosomworth, M.; Clifton, I.; Peckham, D. G.; Conway, S. P. Measurement of Urinary N-Acetyl- β-D-Glucosaminidase in Adult Patients with Cystic Fibrosis: Before, during and after Treatment with Intravenous Antibiotics. *J. Cyst. Fibros.* **2007**, *6* (1), 67–73. https://doi.org/10.1016/j.jcf.2006.05.013.

(23) Jiang, C.; Qi, C.; Sun, K.; Xia, L.; Xue, W.; Huang, Y. Diagnostic Value of N-Acetyl-β-D-Glucosaminidase for the Early Prediction of Acute Kidney Injury after Percutaneous Nephrolithotripsy. *Exp. Ther. Med.* **2013**, *5* (1), 197–200. https://doi.org/10.3892/etm.2012.737.