Moleculin

Developing ground-breaking therapies
for highly challenging diseases

April 16, 2020
Investor Conference Call to Discuss the COVID-19 Potential for our Drug Candidate WP1122
(Nasdaq: MBRX)

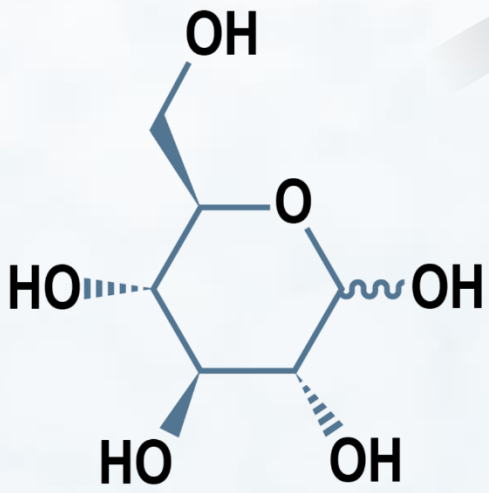
Disclaimer

All statements contained herein other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, and our objectives for future operations, are forward-looking statements. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," and similar expressions are intended to identify forward looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including those discussed under Item 1A. "Risk Factors" in our most recently filed Form 10-K filed with the Securities and Exchange Commission ("SEC") and updated from time to time in our Form 10-Q filings and in our other public filings with the SEC. Any forward-looking statements contained in this release speak only as of its date. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the future events and trends discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward looking statements. More detailed information about Moleculin is set forth in our filings with the Securities and Exchange Commission. Investors and security holders are urged to read these documents free of charge on the SEC's web site at http://www.sec.gov.

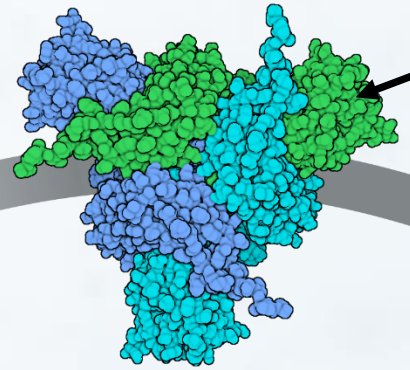
WP1122 COVID-19 Opportunity

- Viruses depend on glycolysis and glycosylation for infectivity and replication
- Glycolysis and glycosylation can be disrupted by using a glucose decoy known as 2-DG
- While 2-DG has been shown to be effective in vitro, its lack of drug-like properties makes it ineffective as a drug in humans
- WP1122 appears to solve 2-DG's problem by creating a prodrug of 2-DG that reaches much higher tissue/organ concentrations than 2-DG alone

Viruses are Highly Dependent on Glucose



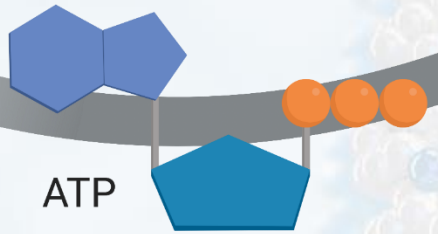
D-Glucose

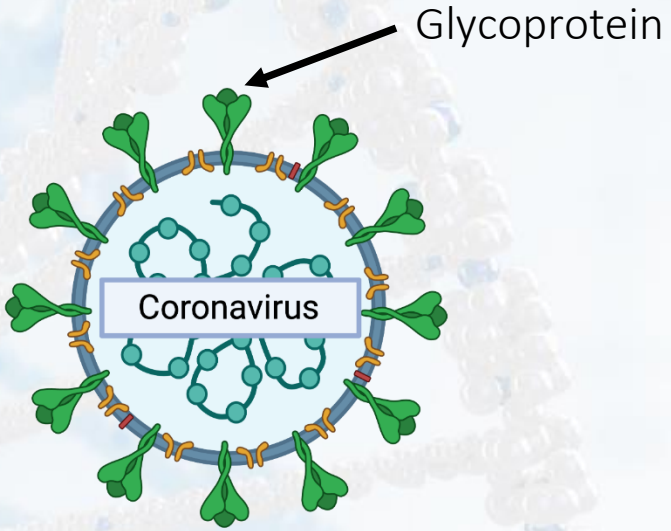


Glycosylation

2 Different Processes

Glycolysis





Glucose provides energy in the form of adenosine tri-phosphate (ATP) to viral host cells via glycolysis, as well as enabling glycan formation supporting creation of glycoproteins during glycosylation.

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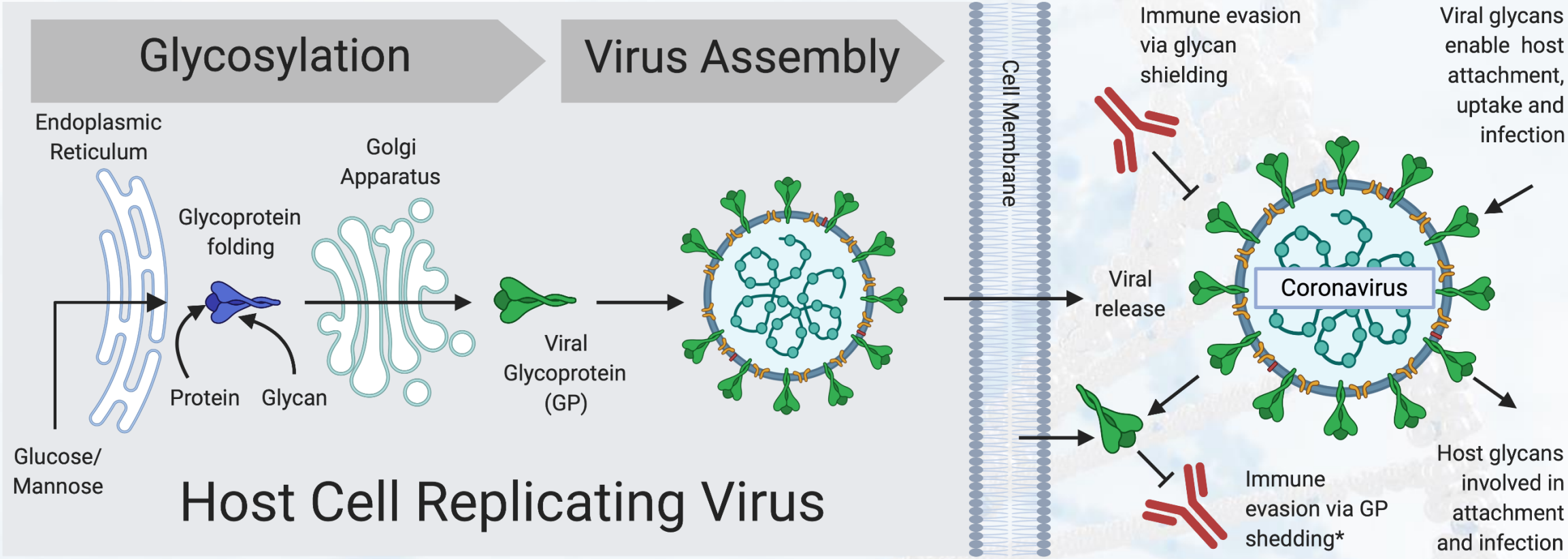
Glucose Plays a Critical Role in Glycosylation



Enveloped viruses depend on glycosylation, which begins by hijacking the host cell secretory pathway, where combinations of sugar molecules (including glucose and mannose) called "glycans" are combined with proteins, as "folding" provides 3-dimensional structure. These viral "glycoproteins" mediate the assembly and budding of new virions. The host's immune system can be evaded through "shedding" of these glycoproteins (* for some viruses, not yet confirmed for coronaviruses) and through "glycan shielding." Glycans are crucial for viral attachment and infection of host cells. – Bagdonaite I., et al. Global aspects of viral glycosylation. Glycobiology. 2018, vol. 28, no. 7, 443–467 doi: 10.1093/glycob/cwy021.

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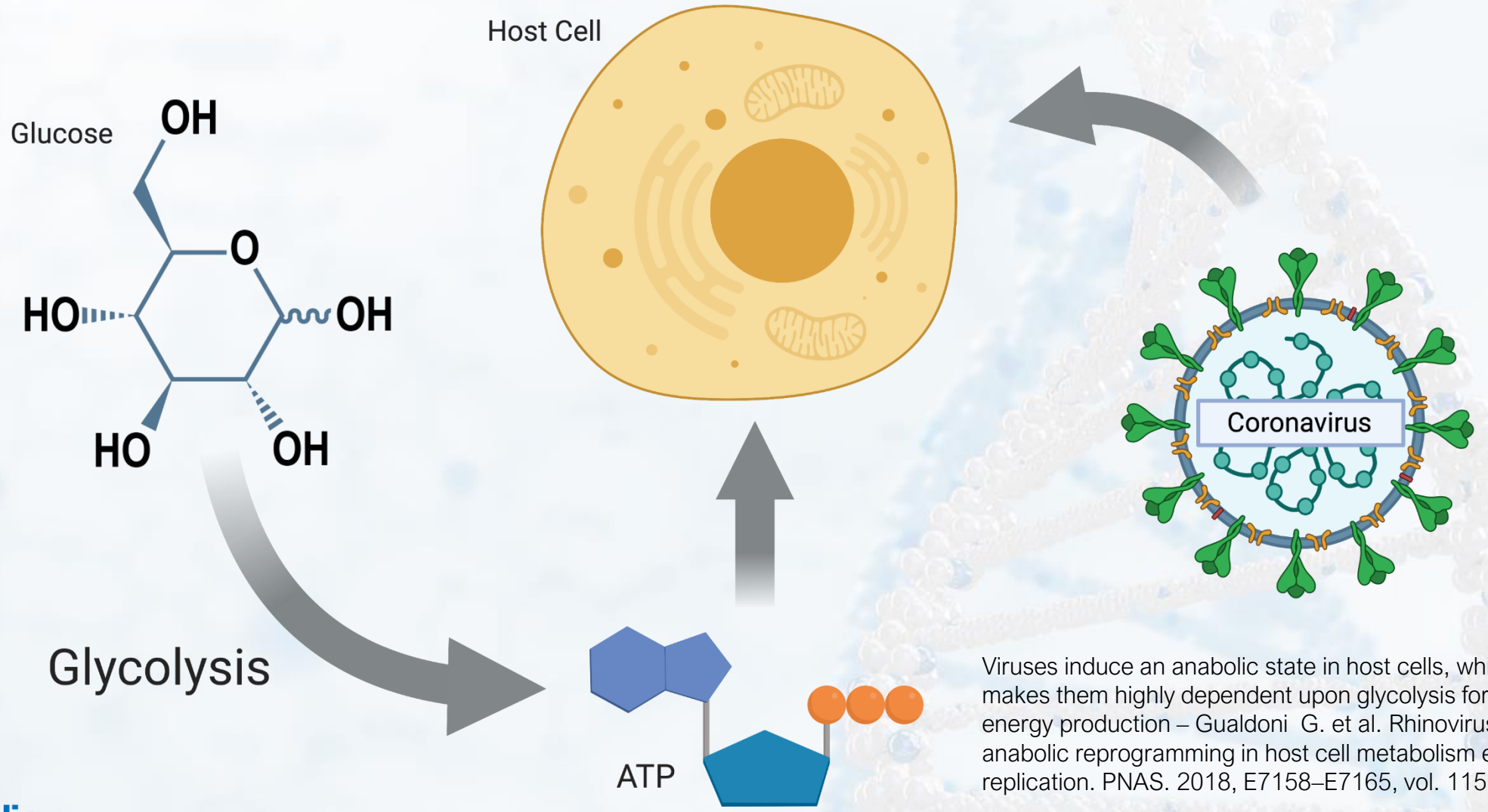
Viruses Upregulate Host Cell's Glycolysis



Viruses induce an anabolic state in host cells, which in turn makes them highly dependent upon glycolysis for adequate energy production – Gualdoni G. et al. Rhinovirus induces an anabolic reprogramming in host cell metabolism essential for viral replication. PNAS. 2018, E7158–E7165, vol. 115, no. 30

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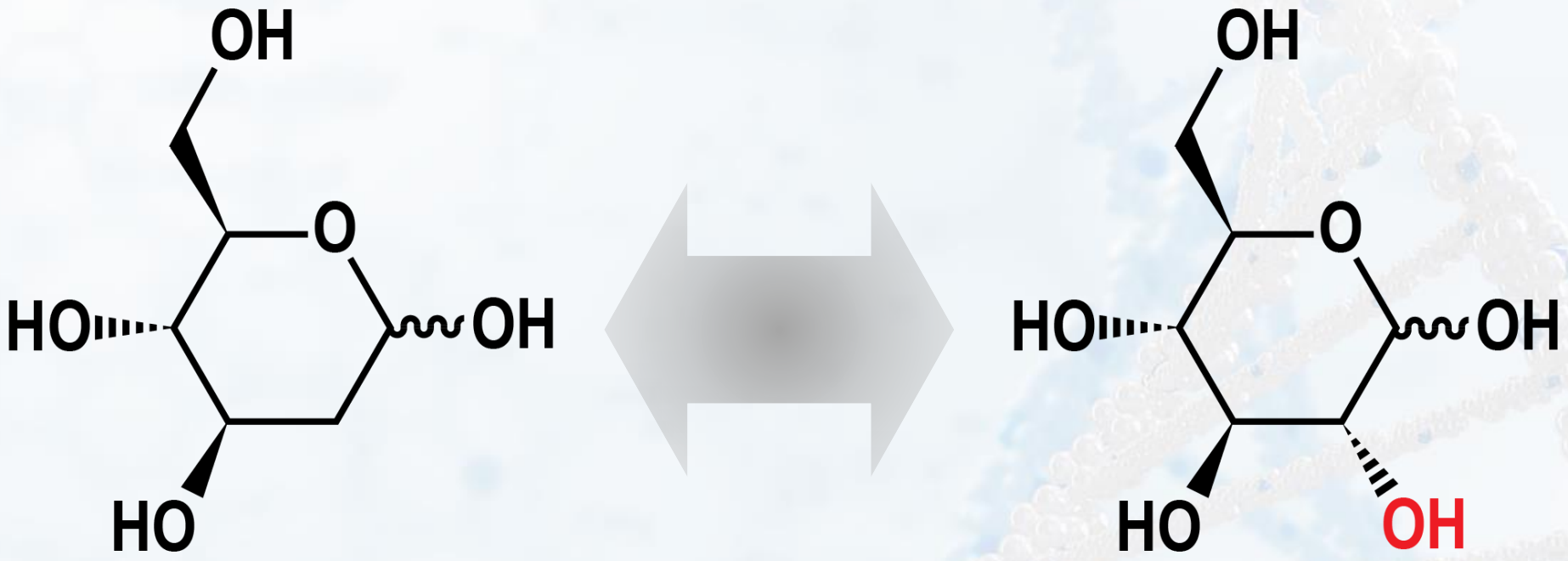
2-DG is a Glucose Decoy



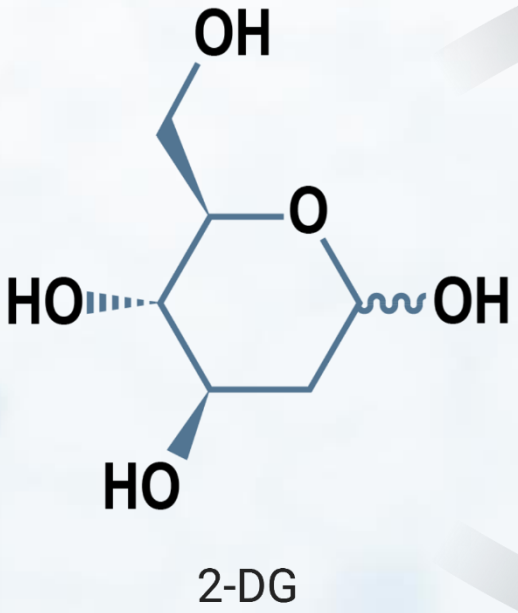
2-Deoxy-D-Glucose

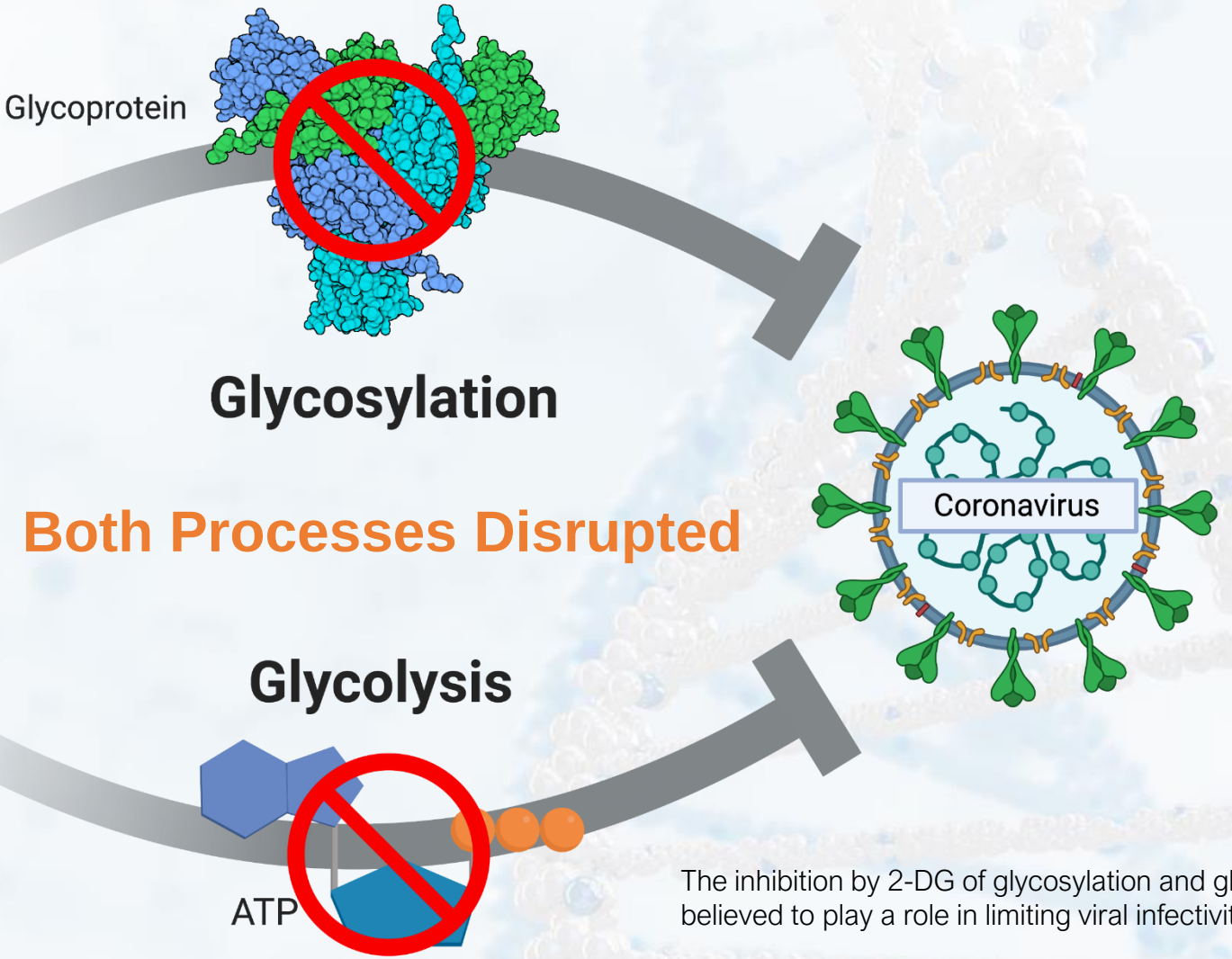
(2-DG)

D-Glucose

2-DG appears to the body to be natural glucose, but its lack of one hydroxyl group (shown in red on D-Glucose above) means that 2-DG will not convert into energy via glycolysis and it will not form the proper building-blocks for glycan formation during glycosylation.

2-DG Disrupts Both Glycosylation and Glycolysis





The inhibition by 2-DG of glycosylation and glycolysis are both believed to play a role in limiting viral infectivity and replication.

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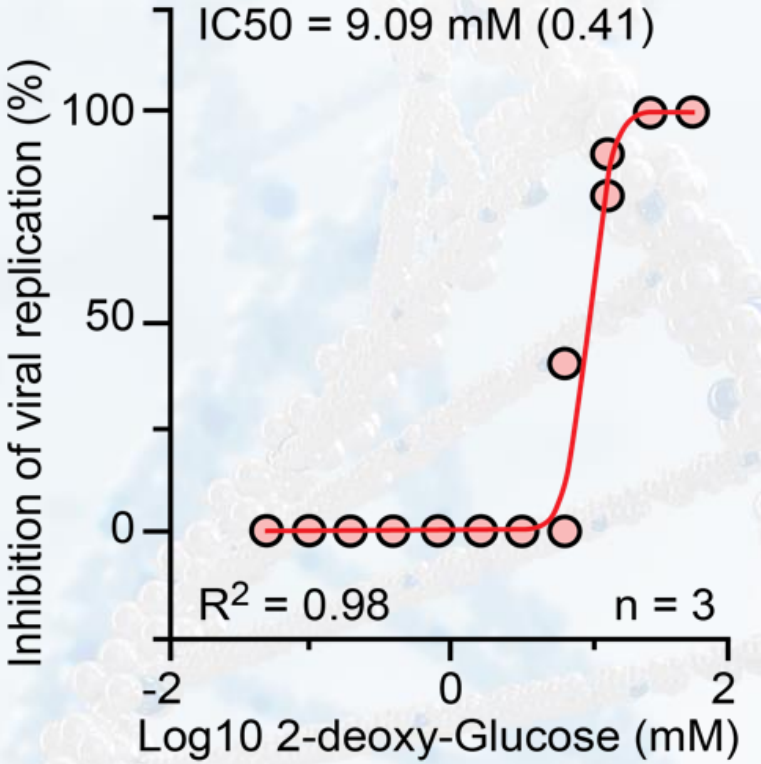
2-DG Has Well-Documented Anti-Viral Properties

- Rhinovirus
- Herpesvirus
- Papillomavirus
- Semliki Forest virus
- Dengue virus
- Porcine epidemic diarrhea virus

- Gualdoni G. et al. Rhinovirus induces an anabolic reprogramming in host cell metabolism essential for viral replication. PNAS. 2018, E7158–E7165, vol. 115, no. 30
- Schmidt M. et al. Interference of Nucleoside Diphosphate Derivatives of 2-Deoxy-D-glucose with the Glycosylation of Virus-Specific Glycoproteins in vivo. Eur. J. Biochem. 70, 55-62 (1976).
- Leung H. J., Duran, E. M., Kurtoglu, M., Andreansky, S., Lampidis, T. J., et al. (2012) Activation of the unfolded protein response by 2-deoxy-D-glucose inhibits kaposi's sarcoma-associated herpesvirus replication and gene expression. Antimicrob. Agents Chemother. 56, 5794–5803
- Maehama, T., Patzelt, A., Lengert, M., Hutter, K. J., Kanazawa, K., et al. (1998) Selective down-regulation of human papillomavirus transcription by 2-deoxyglucose. Int. J. Cancer. 76, 639–646.
- Fontaine K, et al. Dengue Virus Induces and Requires Glycolysis for Optimal Replication. Journal of Virology Jan 2015, 89 (4) 2358-2366. DOI: 10.1128/JVI.02309-14
- Wang Y., et al. Triggering unfolded protein response by 2-Deoxy-D-glucose inhibits porcine epidemic diarrhea virus propagation. Antiviral Research 106 (2014) 33–41.

2-DG Inhibition Now Demonstrated in SARS-CoV-2

2-DG completely stops replication of SARS-CoV-2 in vitro in human Caco-2 cells.



Effect of in vitro incubation of non-cytotoxic levels of 2-DG in Caco-2 cells on viral replication of SARS-CoV-2

Based on research conducted at The Institute of Biochemistry at Goethe University Frankfurt reported in an unreviewed article recently submitted to NatureResearch (https://www.researchsquare.com /article/rs-17218/v1) by Bojkova, D et al. March 11, 2020; DOI: 10.21203/rs.3.rs-17218/v1.

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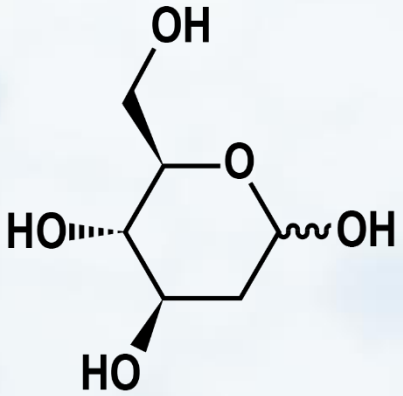
2-DG Is Considered Safe and Well-Tolerated in Humans

- Tested in over 100 patients in multiple clinical trials (7 cited here)
- Phase 2 clinical trial conducted at 63 mg/kg
- The most common adverse events were fatigue, sweating, dizziness and nausea mimicking the hypoglycemic symptoms expected from 2-DG administration
- The most significant adverse effects noted at 63-88 mg/kg doses were reversible hyperglycemia, gastrointestinal bleeding and reversible QTc prolongation

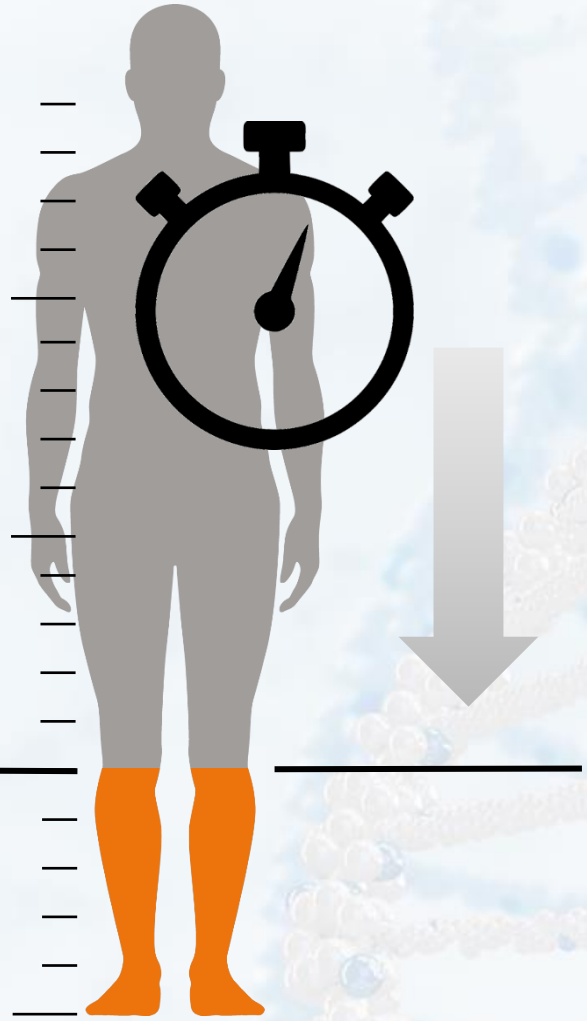
- Raez L.E., et al. "A phase I dose-escalation trial of 2-deoxy-D-glucose alone or combined with docetaxel in patients with advanced solid tumors." Cancer Chemother Pharmacol. 2013 Feb;71(2):523-30. doi: 10.1007/s00280-012-2045-1.
- Laszalo J, et al. "The effect of 2-DG infusions on lipid and carbohydrate metabolism in man." J Clin Invest 1960;40:171-6.
- Thompson DA, et al. "Thermoregulatory and related responses to 2-deoxy-D-glucose administration in humans." Am J Physiol. 1980 Sep;239(3):R291-5.
- Mohanti BK, et al. "Improving cancer radiotherapy with 2-deoxy-D-glucose: phase I/II clinical trials on human cerebral gliomas." Int J Radiat Oncol Biol Phys. 1996 Apr 1;35(1):103-11.
- Singh D, et al. "Optimizing Cancer Radiotherapy with 2-DeoxyD-Glucose." Strahlenther Onkol (2005) 181: 507.
- Murugesan K, et al. "Phase I trial of 2-deoxyglucose for treatment of advanced solid tumors and hormone refractory prostate cancer: A pharmacokinetics (PK) assessment." Proceedings: AACR 101st Annual Meeting 2010-- Apr 17-21, 2010; Washington, DC.
- Stein M, et al. "Targeting tumor metabolism with 2-deoxyglucose in patients with castrate-resistant prostate cancer and advanced malignancies." Prostate. 2010 Sep 15;70(13):1388-94.

Unfortunately, 2-DG Lacks Drug-Like Properties

2-DG's lack of drug-like properties limits its in vivo performance.



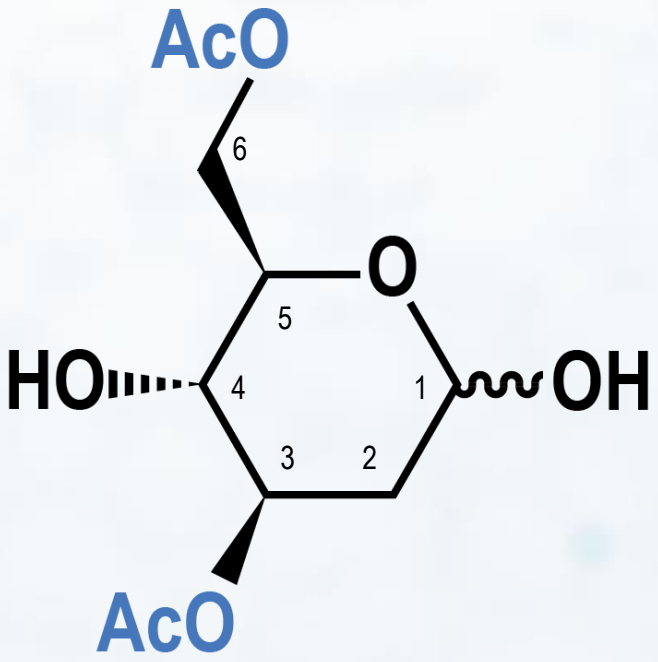
2-DG



Short half-life,
Rapidly metabolized,
Poor tissue/organ uptake and retention

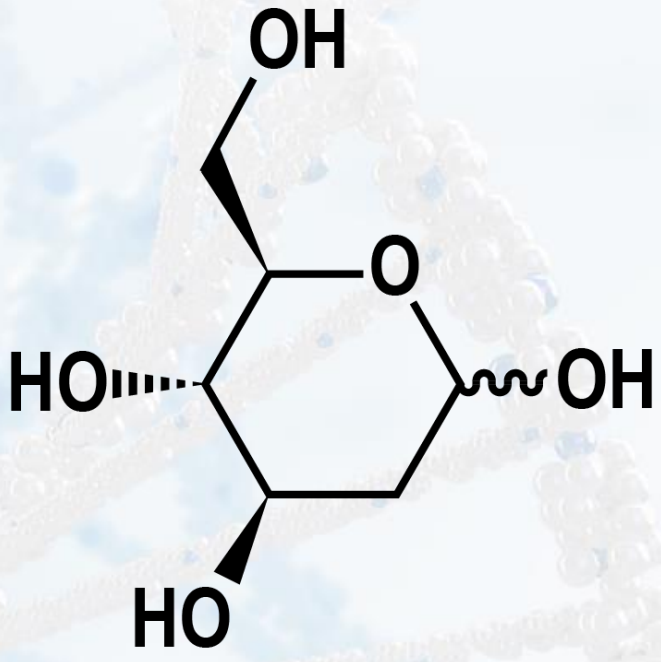
We believe 2-DG's performance in humans is limited by its lack of drug-like properties. Because it is rapidly metabolized, it has inadequate tissue/organ distribution and retention.

WP1122 is a Prodrug of 2-DG



WP1122

WP1122 metabolizes to 2-DG



2-Deoxy-D-Glucose (2-DG)

The presence of two acetyl groups (in blue) in WP1122 forms esters with hydroxyl groups at positions C-3 and C-6 and greatly enhances its tissue/organ uptake and retention.

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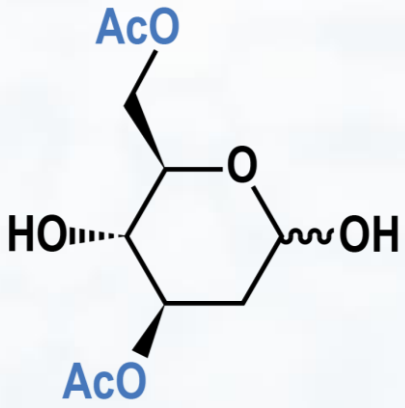
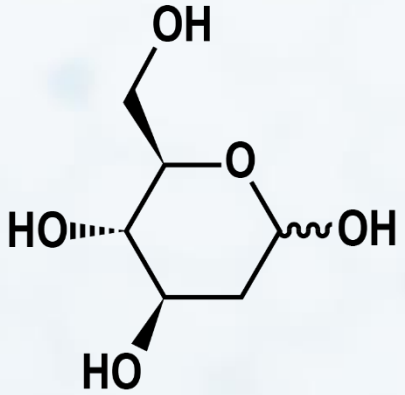
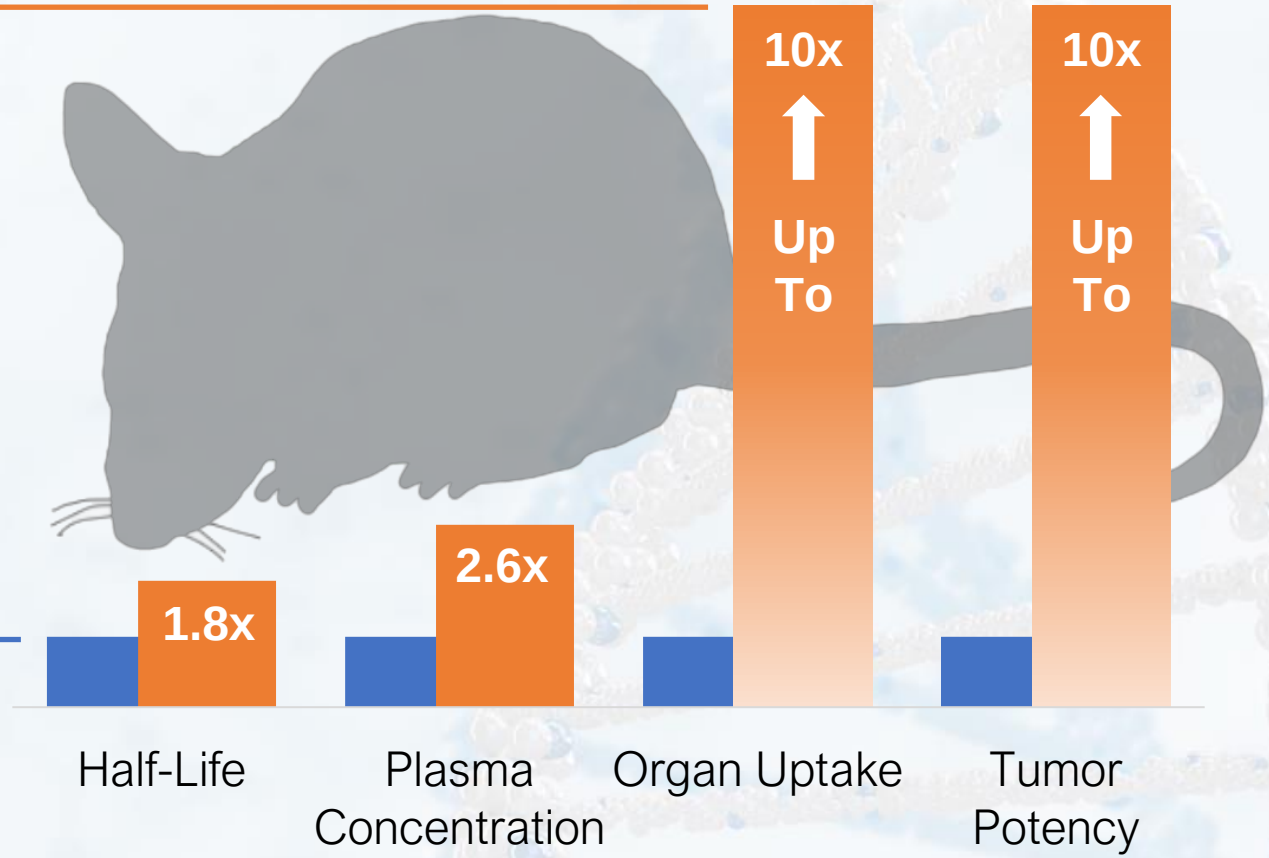
WP1122 Significantly Outperforms 2-DG in animal models





2-DG Generated from WP1122

2-DG



Zielinski R, et al. “Preclinical evaluation of WP1122, a 2-DG prodrug and inhibitor of glycolysis.” Proceedings: Symposia on Cancer Research 2017 Cancer Metabolism, Houston, TX, 10/2017.

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Summary

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