UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): June 8, 2022

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham, New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Tonix Pharmaceuticals Holding Corp. (the "Company") announced two presentations (the "Presentations") entitled "*Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox"* and *"The virus-host Interface: A treasure trove of novel antiviral targets"* by faculty of the Department of Cell Biology, University of Alberta and scientists at the Company, at the 4th Symposium of the Canadian Society for Virology held on June 5, 2022, in Edmonton, Alberta, Canada. Copies of the press releases that discuss these matters are filed as Exhibits 99.01 and 99.02 hereto and incorporated herein by reference. The Presentations, which may contain nonpublic information, are filed as Exhibits 99.03 and 99.04 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01, 99.02, 99.03 and 99.04 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 8.01 Other Events.

On June 8, 2022, the Company announced data included in a poster (the "Poster") entitled, "*Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox,*" which describes data from animals vaccinated with the Company's TNX-801 live virus vaccine product candidate to protect against monkeypox and smallpox. The Poster reports that all animals (eight of eight) vaccinated with TNX-801 were fully protected with sterilizing immunity from a challenge with intra-tracheal monkeypox. The vaccinations with TNX-801 were well tolerated. Synthetic horsepox virus is the basis for the Company's TNX-801 vaccine candidate and for the Company's Recombinant Pox Virus (RPV) platform to protect against other pathogens, including SARS-CoV-2.

Also on June 8, 2022, the Company announced data presented by Professor Tom Hobman, Ph.D., Professor, Department of Cell Biology, The University of Alberta, in a presentation entitled, *"The virus-host Interface: A treasure trove of novel antiviral targets,"* showing that three different Wnt/β-Catenin inhibitor drug candidates decreased lung infection in an animal model of SARS-CoV-2 infection. The set of Wnt/β-Catenin inhibitors tested include drugs that have been previously studied in humans for other indications, including one drug that is approved by the U.S. Food and Drug Administration. Professor Hobman believes that reducing β-Catenin levels with Wnt-inhibitor drugs induces peroxisome proliferation and enhances the interferon response. Previously, SARS-CoV-2 was shown to be sensitive to inhibition by interferon. Professor Hobman reported that Wnt/β-Catenin inhibitor and peroxisome inducing drugs also inhibit Zika virus and Mayaro virus in cell culture. The Company sponsored Professor Hobman's research involving Wnt/β-Catenin signaling pathway inhibitors as broad-spectrum antivirals and has licensed the technology from the University of Alberta.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated June 8, 2022
99.02	Press release of the Company, dated June 8, 2022
99.03	Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox
99.04	The virus-host Interface: A treasure trove of novel antiviral targets
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: June 8, 2022

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Tonix Pharmaceuticals Announces Presentation on TNX-801 Vaccine Protection Against Monkeypox at the 4th Symposium of the Canadian Society for Virology

Poster Presentation Includes Preclinical Data from Tonix's Program to Develop a Vaccine for Monkeypox and Smallpox

CHATHAM, N.J., June 8, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that Ryan Noyce, Ph.D.,and David Evans, Professor, Department of Cell Biology, University of Alberta, together with scientists from Tonix presented data from a research collaboration between Tonix Pharmaceuticals and The University of Alberta in a poster presentation at the 4th Symposium of the Canadian Society for Virology held in Edmonton, Alberta, Canada on June 5, 2022. Copies of the poster are available on the Tonix Pharmaceuticals corporate website at www.tonixpharma.com.

The poster titled, *"Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox,* describes data from animals vaccinated with TNX-801[1] to protect against monkeypox. The poster presentation reports that all animals (eight of eight) vaccinated with TNX-801 were fully protected with sterilizing immunity from a challenge with intra-tracheal monkeypox. The vaccinations with TNX-801 were well tolerated. Synthetic horsepox virus is the basis for the Company's TNX-801 vaccine in development to protect against monkeypox and smallpox and for the Company's Recombinant Pox Virus (RPV) platform to protect against other pathogens, including SARS-CoV-2.

"Our research work, in collaboration with Dr. Noyce and Professor Evans at The University of Alberta, shows that vaccination with TNX-801 has the ability to protect against monkeypox infection," said Seth Lederman, M.D., President and Chief Executive Officer. "Monkeypox infection of humans was rare during the time people were vaccinated to protect against smallpox. After the eradication of smallpox, vaccination with live-virus vaccinia was stopped in most of the world. Monkeypox cases have been rising in Africa for several years. Very recently a strain of monkeypox from West Africa has caused clusters of monkeypox cases in many countries outside of Africa. We believe that vaccination with live-virus vaccines like TNX-801 has the potential to control monkeypox again."

About TNX-801, TNX-1840 and TNX-1850

TNX-801 is a live virus vaccine based on synthesized horsepox[2,3]. Tonix is developing TNX-801 for percutaneous administration as a vaccine to protect against monkeypox and smallpox. Tonix has previously reported positive data from a monkeypox challenge study in non-human primates[4]. Tonix is also developing TNX-1840 and TNX-1850 (horsepox-based live virus vaccines) for the prevention of COVID-19. TNX-1840 and TNX-1850 are designed to express the spike protein from the omicron and BA.2 variants of SARS-CoV-2, respectively. Tonix has previously reported positive data from a SARS-CoV-2 challenge study in non-human primates in which animals were vaccinated with TNX-1800, a horsepox-based vaccine expressing spike protein from the Wuhan strain[5]. Tonix's TNX-801 was synthesized[2] based on the sequence of the 1976 natural isolate Mongolian horsepox clone MNR-763. Molecular analysis of DNA sequences suggests that TNX-801 is closer than modern smallpox vaccines to the vaccine discovered and disseminated by Dr. Edward Jenner in 1798[6-8]. For example, recent studies[9,10] have shown approximately 99.7% colinear identity between TNX-801 and the circa 1860 U.S. smallpox vaccine VK05.[11] The small

---

plaque size in culture of TNX-801 appears identical to the U.S. Centers for Disease Control publication of the natural isolate[12]. Relative to vaccinia, horsepox has substantially decreased virulence in mice[2]. Dr. Edward Jenner invented vaccination in 1798 and the procedure was called "vaccination" because 'cow' is 'vacca' in Latin and the inoculum material was initially obtained from lesions on the udders of cows affected by a mild disease known as cowpox. However, Dr. Jenner suspected that cowpox originated from horses.8 Subsequently, Dr. Jenner and others immunized against smallpox using material directly obtained from horses. The use of vaccines from horses was sometimes called 'equination' from the Latin 'equus' which means 'horse'[13]. Equination and vaccination were practiced side-by-side in Europe[13,14].

About the Recombinant Pox Virus (RPV) Platform

Horsepox virus and vaccines based on its use as a vector are live replicating viruses that elicit strong immune responses. Live replicating orthopoxviruses, like vaccinia or horsepox, can be engineered to express foreign genes and have been exploited as platforms for vaccine development because they possess; (1) large packaging capacity for exogenous DNA inserts, (2) precise virus-specific control of exogenous gene insert expression, (3) lack of persistence or genomic integration in the host, (4) strong immunogenicity as a vaccine, (5) ability to rapidly generate vector/insert constructs, (6) manufacturable at scale, and (7) ability to provide direct antigen presentation. Relative to vaccinia, horsepox has substantially

decreased virulence in mice2. Horsepox-based vaccines are designed to be single dose, vial-sparing vaccines, that can be manufactured using conventional cell culture systems, with the potential for mass scale production and packaging in multi-dose vials. Tonix's TNX-801 and RPV vaccine candidates are administered percutaneously using a two-pronged, or "bifurcated" needle. The major cutaneous reaction or "take" to vaccinia vaccine was described by Dr. Edward Jenner in 1796 and has been used since then as a biomarker for protective immunity to smallpox, including in the World Health Organization's (WHO) accelerated smallpox eradication program that successfully eradicated smallpox in the 1960's. The "take" is a measure of functional T cell immunity validated by the eradication of smallpox, a respiratory-transmitted disease caused by variola.

About Monkeypox and Smallpox

Monkeypox[15] and smallpox[16] are diseases in humans called by the monkeypox and smallpox (or variola) viruses, respectively. Monkeypox and variola are closely related orthopox viruses. Vaccination against smallpox with live virus vaccines based on horsepox or vaccinia protects against monkeypox. After routine smallpox vaccination was stopped in about 1970, monkeypox has become a growing problem in Africa. Recently approximately 300 cases have been identified outside of Africa.[17] Smallpox is considered eradicated, but there are concerns about malicious reintroduction.

About Tonix Pharmaceuticals Holding Corp.[1]

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product

---

candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the first quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix expects to initiate a Phase 2 study in Long COVID in the second quarter of 2022. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the second quarter of 2022. TNX-1300 has been granted Breakthrough Therapy Designation by the FDA. Finally, TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the second half of 2022. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan-Drug Designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500 which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox called TNX-801, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850, which are live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform.

[1]All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.

[2]Noyce RS, et al. (2018) PLoS One. 13(1):e0188453

[3]Tulman ER, et al. (2006) J Virol. 80(18):9244-58.PMID:16940536

[4]Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox Presented as a poster at the American Society of Microbiology BioThreats Conference – January 29, 2020, Arlington, VA. (https://content.equisolve.net/tonixpharma/media/10929ac27f4fb5f5204f5cf41d59a121.pdf)*

[5]Tonix Press Release March 16, 202a https://ir.tonixpharma.com/news-events/press-releases/detail/1255/tonix-pharmaceuticals-reports-positive-covid-19-vaccine

[6]Schrick L et al. N Engl J Med. (2017) 377:1491.

[7]Qin et al. J. Virol. 89:1809 (2015).

[8]Jenner E. "An Inquiry Into the Causes and Effects of the Variolae Vaccinae: A Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire, and Known by the Name of the Cow Pox." London: Sampson Low, 1798.

[9]Brinkmann A et al, Genome Biology (2020) 21:286 https://doi.org/10.1186/s13059-020-02202-0

[10]Duggan A et al. Genome Biology (2020) 21:175 https://doi.org/10.1186/s13059-020-02079-z

[11]Tonix press release. Dec 4, 2020 https://ir.tonixpharma.com/news-events/press-releases/detail/1236/vaccine-genome-researchers-report-99-7-colinear-identity

[12]Trindale GS et al. Viruses (2016) (12). Pii: E328. PMID:27973399

[13]Esparza E, et al Vaccine. (2017) 35(52):7222-7230.

[14]Esparza J et al. Vaccine. (2020); 38(30):4773-4779.

[15]www.cdc.gov/poxvirus/monkeypox/about.html

[16] *www.cdc.gov/smallpox/research/*

---

[17] *Mandavilli, A. The New York Times. May 26, 2020. "Who is protected against monkeypox"*

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the "SEC") on March 14, 2022, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

Contacts

Jessica Morris (corporate)
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 799-8599

Olipriya Das, Ph.D. (media)
Russo Partners
Olipriya.Das@russopartnersllc.com
(646) 942-5588

Peter Vozzo (investors)
ICR Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

Exhibit 99.02

Tonix Pharmaceuticals Announces Presentation of Licensed Antiviral Drug Technology at the 4 th Symposium of the Canadian Society for Virology

Oral Presentation Describes Activity of Wnt/β-Catenin Signaling Pathway Inhibitors Against SARS-CoV-2 in Cell Culture and in an Animal Model

CHATHAM, N.J., June 8, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that Tom Hobman, Ph.D., Professor, Department of Cell Biology, University of Alberta, presented data from his laboratory at The University of Alberta as a keynote presentation at the 4th Symposium of the Canadian Society for Virology held in Edmonton, Alberta, Canada on June 5, 2022. The oral presentation titled,*"The virus-host Interface: A treasure trove of novel antiviral targets,"* includes research sponsored by Tonix Pharmaceuticals focused on the development and testing of Wnt/β-Catenin signaling pathway inhibitors as broad-spectrum antivirals against SARS-CoV-2 and other emerging viruses. Tonix has previously announced that it exercised an option to license the antiviral technology platform A copy of the presentation is available on the Tonix Pharmaceuticals corporate website at www.tonixpharma.com.

"We are excited by the progress of Professor Hobman and his colleagues at The University of Alberta on the further testing of Wnt/β-Catenin signaling pathway inhibitors as broad-spectrum antivirals," said Seth Lederman, M.D., President and Chief Executive Officer of Tonix. "Professor Hobman presented data showing that three different Wnt/β-Catenin inhibitor drug candidates decreased lung infection in an animal model of SARS-CoV-2 infection. The set of Wnt/β-Catenin inhibitors tested by Professor Hobman include drugs that have been previously studied in humans for other indications including one drug that is FDA approved. Professor Hobman believes that reducing β-Catenin levels with Wnt-inhibitor drugs induces peroxisome proliferation and enhances the interferon response. Previously, SARS-CoV-2 was shown to be sensitive to inhibition by interferon[2]. Professor Hobman reported that Wnt/β-Catenin inhibitor and peroxisome inducing drugs also inhibit Zika virus (ZIKV) and Mayaro (MAYV) virus in cell culture. Tonix is excited to have sponsored Professor Hobman's research involving Wnt/β-Catenin signaling pathway inhibitors as broad-spectrum antivirals and to have licensed the technology. We look forward to working with Professor Hobman to try to bring one or more of these candidate drugs to clinical testing."

About Tonix Pharmaceuticals Holding Corp.[1]

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the first quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix expects to initiate a Phase 2 study in Long COVID in the second quarter of 2022. TNX-1300 (cocaine

---

esterase) is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the second quarter of 2022. TNX-1300 has been granted Breakthrough Therapy Designation by the FDA. Finally, TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the second half of 2022. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan-Drug Designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500 which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox called TNX-801, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850, which are live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform.

[1] *All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

[2] *Lokugamage, K. G. et al., (2020). Journal of virology, 94 (23), [e01410]. https://doi.org/10.1128/JVI.01410-20*

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the “SEC”) on March 14, 2022, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

Contacts

Jessica Morris (corporate)

Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 799-8599

Olipriya Das, Ph.D. (media)
Russo Partners
Olipriya.Das@russopartnersllc.com
(646) 942-5588

Peter Vozzo (investors)
ICR Westwicke
peter.vozzo@westwicke.com
(443) 213-0505

Exhibit 99.03

Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox

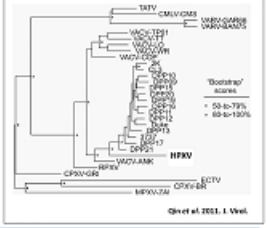
Ryan Noyce[1], Landon Westfall[2], Siobhan Fogarty[3], Karen Gilbert[2], Onesmo Mpanju[4] **Helen Stillwell[3]**, Jose Esparza[5], Fustaka Koide[2], David Evans[1], and Seth Lederman[3]

[1]University of Alberta, [2]Southern Research, [3]Tonix Pharmaceuticals, [4]UNQ Pharma Consulting, [5]Institute of Human Virology, U. of Maryland

Introduction

Despite its eradication, smallpox remains a biothreat. While US military Global Response Force service troops are immunized with clonal, live vaccinia virus (VACV), safety concerns limit its further use in groups like first responders. There is a need for an effective but better tolerated, single dose, live replicating smallpox vaccine. Sequence analysis of polyclonal or old smallpox vaccines indicate a common ancestor with horsepox virus (HPXV)[1], and suggest that modern VACV diverged in the core viral sequence, and in the accumulation of deletions in the left and right inverted terminal repeats (ITRs). However, it is unknown if the early HPXV-like vaccines, which protected against smallpox, exhibited different safety and efficacy profiles compared to modern VACV. To assess the tolerability and vaccine activity of a synthetic/chimeric (sc)HPXV, four groups of macaques were vaccinated either with two different doses of scHPXV, one dose of synthetic VACV (sVACV), or vehicle prior to challenge with monkeypox virus (MPXV).

Figure 1. Phylogenetic relationships between VACV strains and HPXV



Qin et al. 2011. J. Virol.

Figure 2. Similarities between VACV strains and HPXV:

Experimental Procedures

scHPXV and sVACV were assembled using synthetic DNA fragments as described previously[2]. A laboratory isolate of VACV was sequenced using Illumina sequencing technologies to obtain a complete genome sequence, including the terminal hairpin sequences and repeat region in the inverted terminal repeat (ITR). This sequence is very similar to VACV [strain ACAM 2000] and has been deposited in Genbank (Accession # **MN974380**). The sVACV genome sequence was also deposited into Genbank (Accession # **MN974381**).

Cynomolgus macaques (4 per group) were vaccinated via scarification using a bifurcated needle with 4x10[8] or 5x10[8] PFU of scHPXV, 8x10[8] PFU of sVACV, or PBS, before challenge 60 days later with 9x10[7] PFU of MPXV (strain Zaire) via the intratracheal (I.t.) route.

Table 1. Experimental Design for scHPXV Dose-Range Finding Study in NHP.

Group	N	Vaccine (Day 0)	Vaccination Dose (PFU)*	Route of Vaccine Administration	IT Challenge Dose (Day 60)
1	4	scHPXV	$4x10^8$	Scarification	$9x10^7$ PFU
2	4	scHPXV	$5x10^8$	Scarification	$9x10^7$ PFU
3	4	sVACV	$8x10^8$	Scarification	$9x10^7$ PFU
4	4	Vehicle	N/A	Scarification	$9x10^7$ PFU

*A second vaccination by scarification (following procedures and dose volume used on day 0) was given to four animals that did not show evidence of a take at the vaccination site by day 7. The re-vaccination of these four animals occurred on day 14.

Figure 3. Treatment Timeline

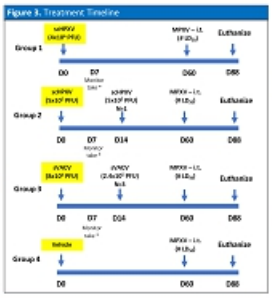


Figure 4. Representative Images of Vaccination Site on Day 7:

Results

Two different doses of scHPXV vaccine were tested: 4 of 4 animals in the $4x10^8$ PFU dose, and 3 of 4 animals in the $5x10^8$ PFU dose groups exhibited a "take" at day 7. A take is a biomarker of protective immunity in immunocompetent recipients receiving live VACV vaccine and has been successfully used in campaigns to prevent smallpox contagion. In the sVACV arm only 1 of 4 animals exhibited a take. The animals that did not present a take were revaccinated on day 14: the one scHPXV animal was revaccinated with $5x10^8$ PFU scHPXV and the 3 sVACV animals were revaccinated with $2.4x10^8$ PFU sVACV. All but one of the sVACV animals subsequently produced a take. After MPXV challenge no lesions were seen in any of the 8 animals vaccinated with scHPXV. One animal in the sVACV arm died from unrelated causes, but while the 3 remaining animals all had takes, 2 still showed lesions by day 69. Symptoms characteristic of systemic monkeypox infections were seen in all 4 vehicle animals by day 69.

scHPXV is Tolerated During Vaccination of Macaques

Figure 5. Weights of Macaques During Vaccination Period

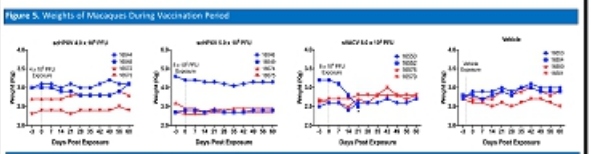
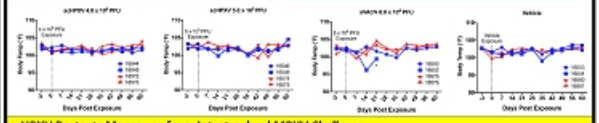


Figure 6. Body Temperature of Macaques During Vaccination Period



scHPXV Protects Macaques from Intratracheal MPXV Challenge

Figure 7. Weight Change

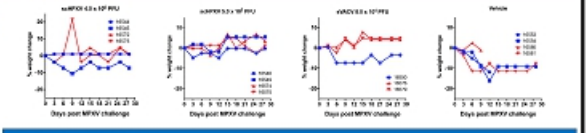
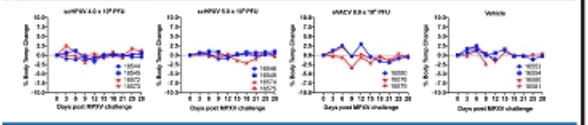
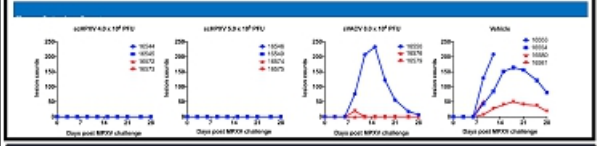


Figure 8. Change in Body Temperature





Conclusions

- HPXV virus is closely related to VACV
- Molecular evolution indicates that HPXV is a primordial strain (with "complete" left and right ITRs).
- HPXV has additional genes, relative to VACV that are mostly involved in host immune interactions
- HPXV likely closer to the vaccine used by Edward Jenner than more recent strains (in terms of left and right ITRs and core viral sequence).
- Tolerability of HPXV at low and high dose is comparable to VACV at low dose.
- Protection of HPXV and VACV was comparable (all 8 HPXV animals and all 3 VACV animals survived and recovered)
- HPXV had higher rates of "take" (4/4 high dose and 3/4 low dose) than VACV (1/3) after a single vaccination.
- "Take" is the major cutaneous reaction that is a biomarker of protective and sterilizing immunity in immunocompetent individuals vaccinated with a live vaccinia virus
- HPXV induced sterilizing immunity (no lesions) in all 8 animals (4 high dose and 4 low dose), while VACV (low dose) provided sterilizing immunity only 1 of 3.

[1]Schrick L et al. N Engl J Med. (2017) 377:1491; [2]Noyce RS et al. PLoS One. (2018) 13:e0188455.

Exhibit 99.04

The virus-host interface: A treasure trove of novel antiviral targets

Tom C. Hobman
Department of Cell Biology,
Li Ka Shing Institute of Virology
University of Alberta

Disclosures

- Received research funding from Tonix Pharmaceuticals
- Licensing agreement with Tonix Pharmaceuticals

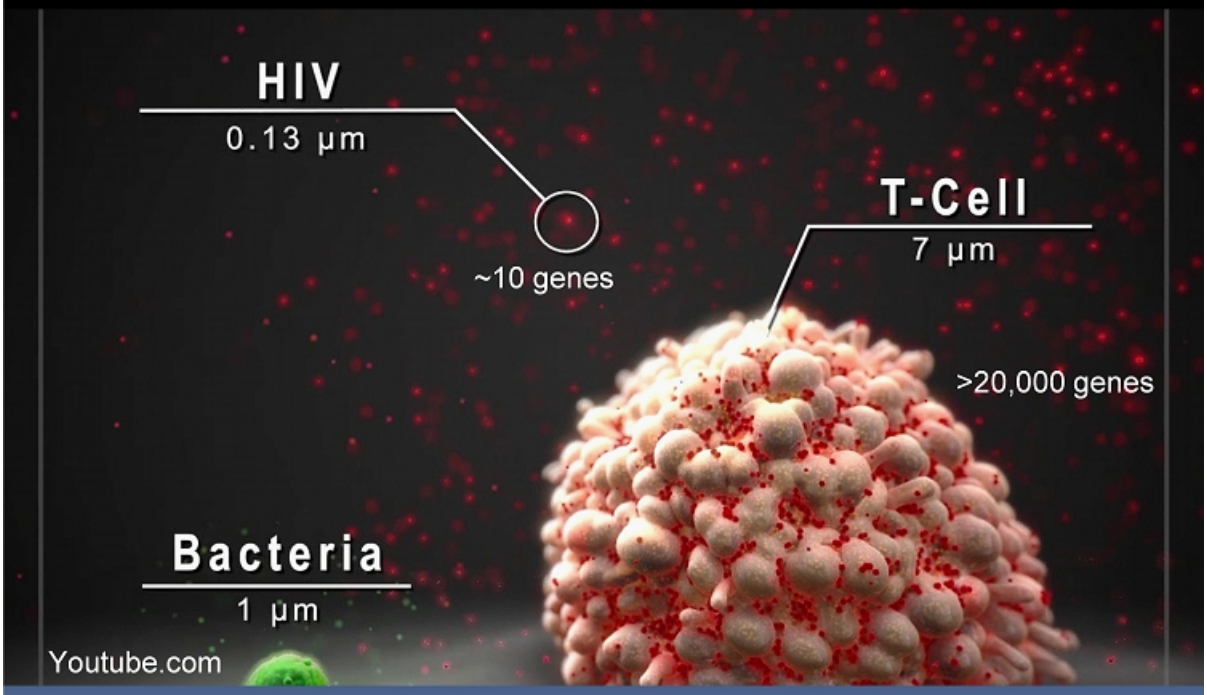
Burden of epidemic/pandemic viruses

- Smallpox virus , influenza virus, Dengue virus, HIV, chikungunya virus, Ebola virus, HCV, HBV, Zika virus, SARS-CoV-2 ….
- Billions of people infected since 19th century
- Hundreds of millions of deaths
- Enormous economic and social impact
  - >$82 trillion for COVID-19

Paucity of antivirals for emerging viruses

- Conventional antivirals target viral proteins
  - Take years to develop
  - Often highly specific
- Vaccines are most effective in preventing viral diseases
  - Highly specific
- Need broad spectrum antivirals as first line of defense against emerging viruses

Taking advantage of the matchup

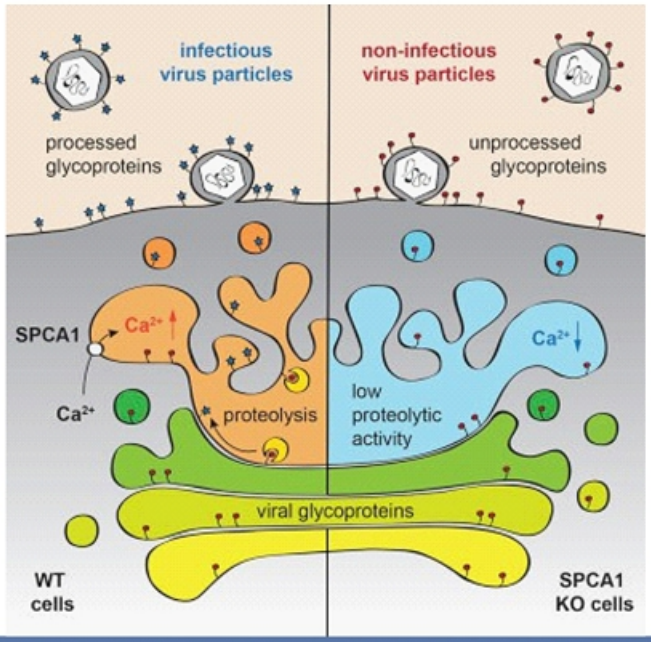


Targeting host-dependency factors is an exciting new frontier for antivirals

- Viruses are wholly reliant on host cellular pathways for replication & assembly
- Vulnerabilities
  - Conserved pathways that can be targeted
    - Multiple viruses affected
  - Less chance of developing resistance

Proof of principle

The calcium pump SPCA1 is required for infectivity of multiple RNA viruses including measles, Dengue, West Nile, Zika and chikungunya viruses

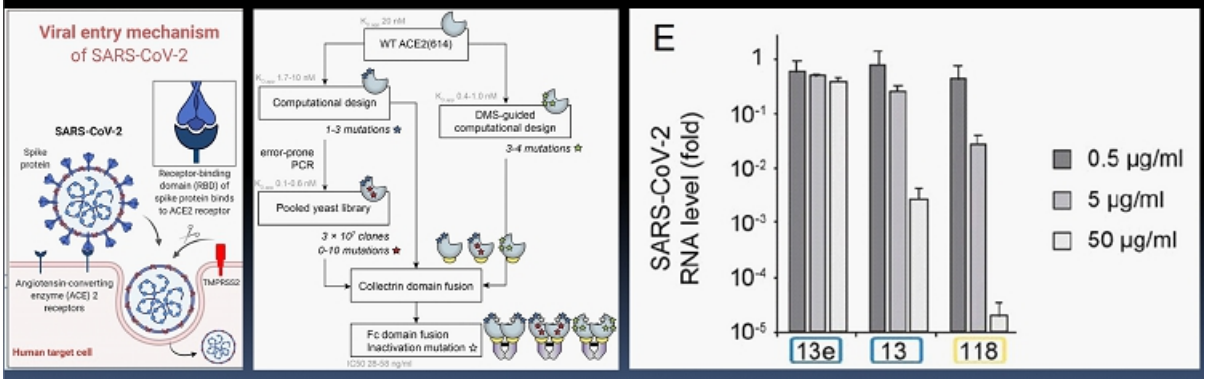


Hoffmann et al, 2017 Cell Host Microbe

Engineered ACE2 receptor traps potently neutralize SARS-CoV-2

Anum Glasgow[a,1], Jeff Glasgow[b,1], Daniel Limonta[c,d], Paige Solomon[b], Irene Lui[b], Yang Zhang[a], Matthew A. Nix[e], Nicholas J. Rettko[b], Shoshana Zha[f], Rachel Yamin[g], Kevin Kao[g], Oren S. Rosenberg[f], Jeffrey V. Ravetch[g], Arun P. Wiita[e], Kevin K. Leung[b], Shion A. Lim[b], Xin X. Zhou[b], Tom C. Hobman[c,d,h], Tanja Kortemme[a], and James A. Wells[b,i,2]

28046–28055 | PNAS | November 10, 2020 | vol. 117 | no. 45



>50,000-fold reduction in SARS-CoV-2 replication

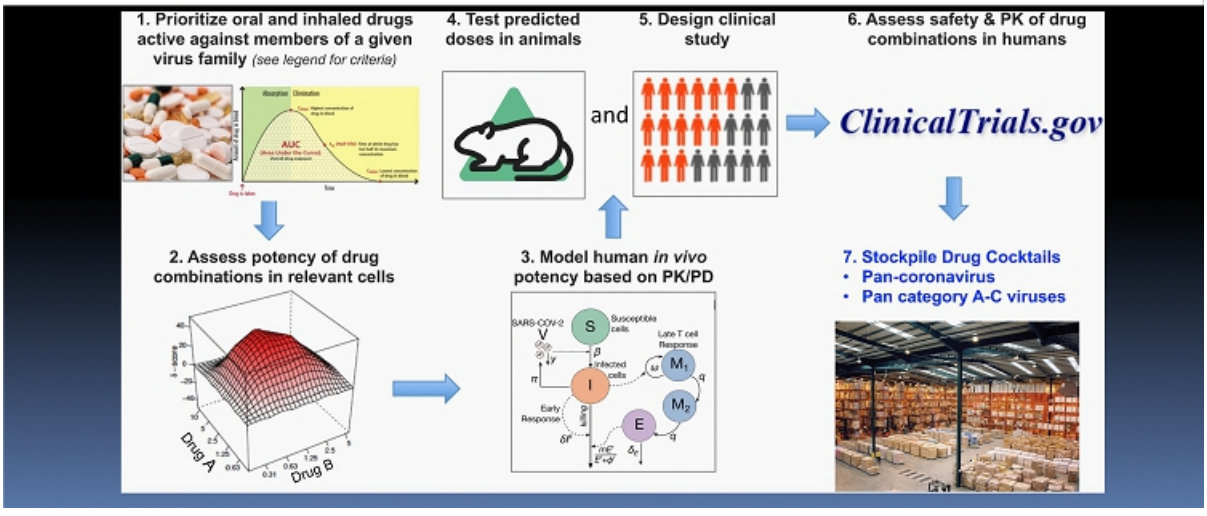
AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

MINIREVIEW

Drug Combinations as a First Line of Defense against Coronaviruses and Other Emerging Viruses

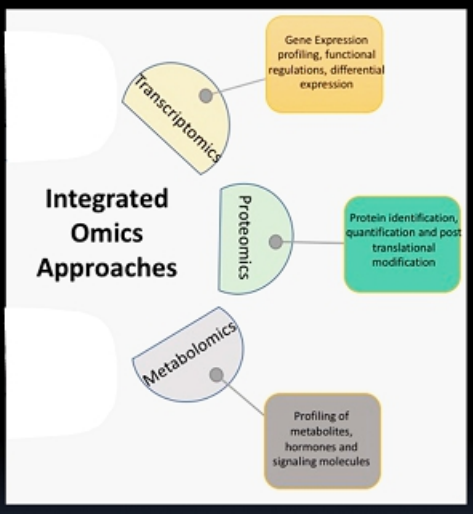
Judith M. White,[a,b] Joshua T. Schiffer,[c,d] Rachel A. Bender Ignacio,[c,d] Shuang Xu,[d] Denis Kainov,[e,f,g] Aleksandr Ianevski,[e,g] Tero Aittokallio,[g,h,i] Matthew Frieman,[j] Gene G. Olinger,[k] Stephen J. Polyak[l,m,n]

"For the present pandemic response, and for future pandemics …. the scientific community must be ready with an arsenal of easily self-administered drugs that can be tested in rapid, efficient clinical trials immediately after the causative viral agent is identified."



Experimental approaches

- Flaviviruses
- Alphaviruses
- HIV
- Coronaviruses



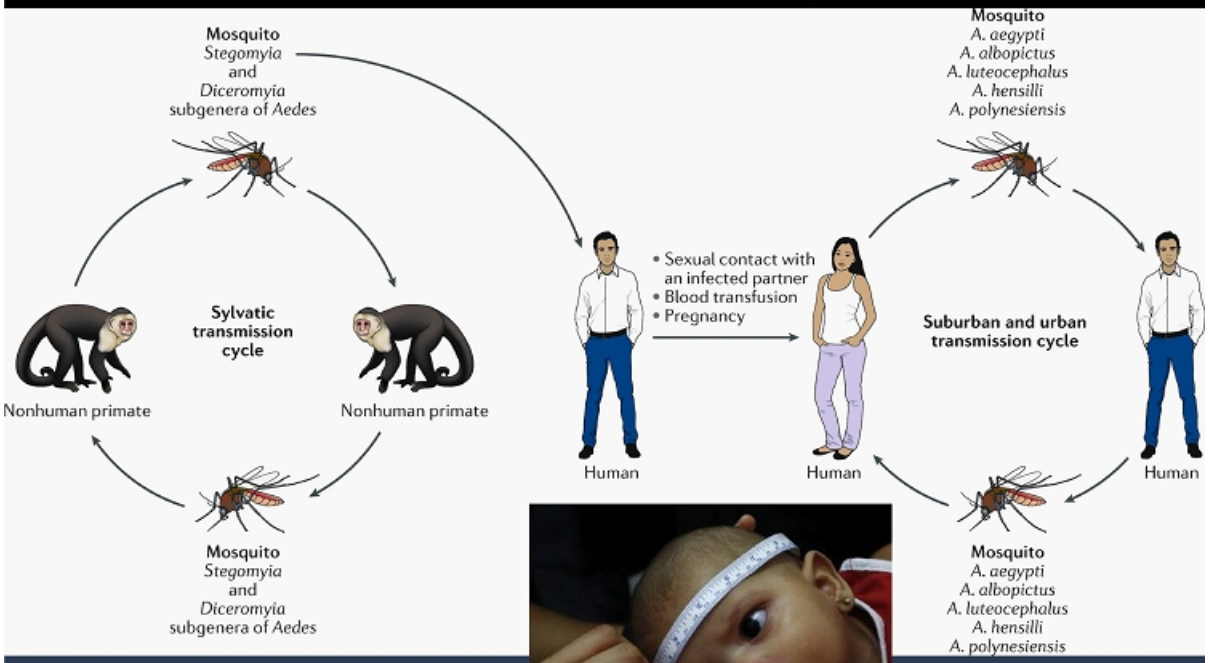
- Determine which cellular pathways are perturbed or activated
- Test effects of pathway agonists/inhibitors on virus replication

---

Zika virus (ZIKV) distribution

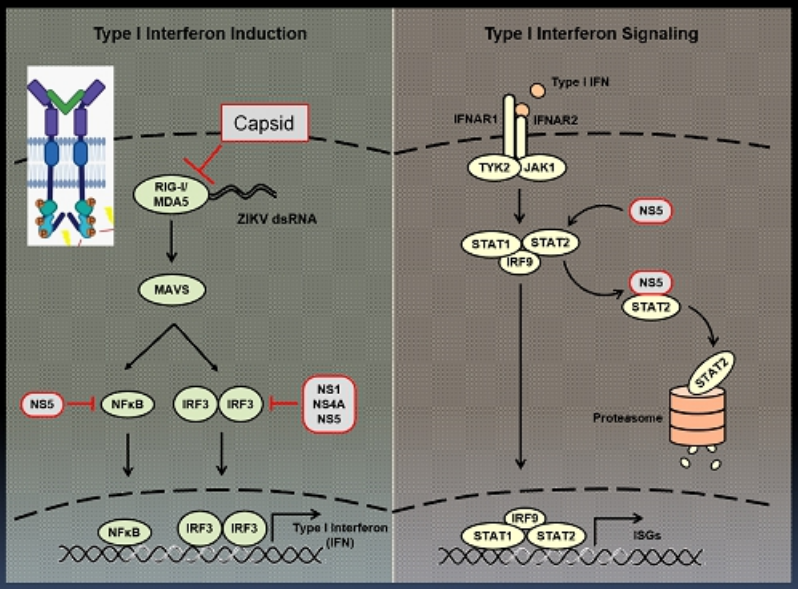
ResearchGate

ZIKV transmission cycles



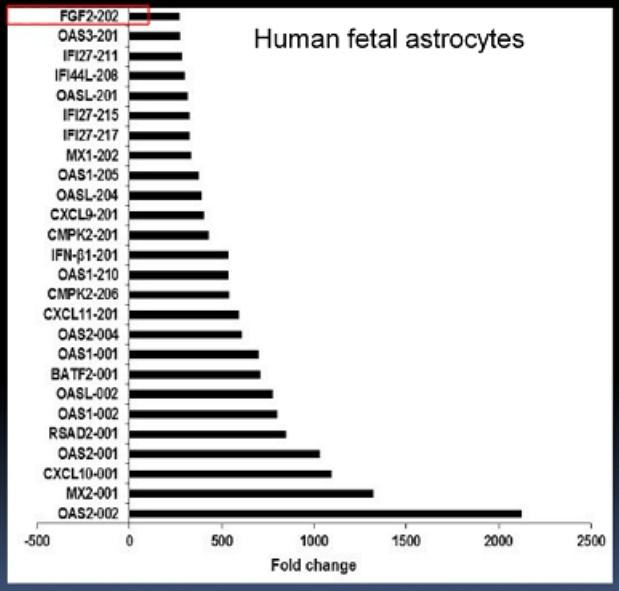
Sharma et al, 2019

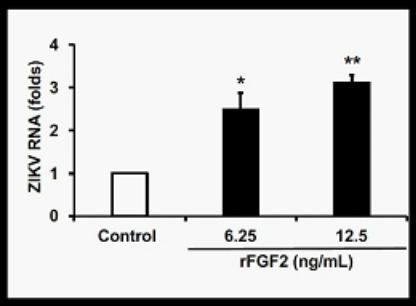
ZIKV causes persistent infection and uses multiple strategies to antagonize the interferon response

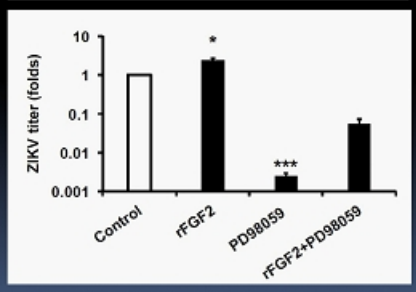


Kumar, Hou et al, 2016; Kumar et al, 2018; Limonta et al, 2019; Airo et al, 2022

Fibroblast growth factor-2 (FGF2) mRNA is upregulated 270-8600X during ZIKV infection



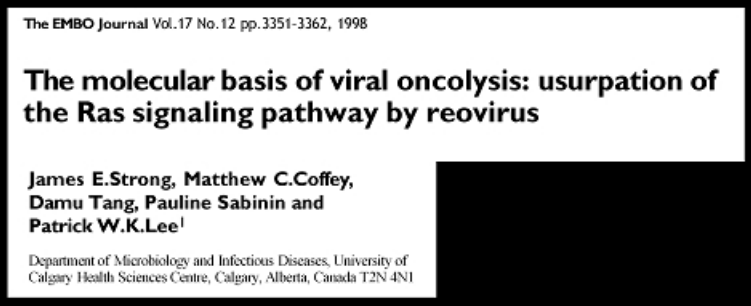




Kumar et al, 2018 (Sertoli cells)
Limonta et al, 2019 (Fetal astrocytes)

- **FGF2 signaling suppresses IFN!**

Canadian pioneers in regulation of the IFN response



The EMBO Journal Vol.17 No.12 pp.3351-3362, 1998

The molecular basis of viral oncolysis: usurpation of the Ras signaling pathway by reovirus

James E.Strong, Matthew C.Coffey, Damu Tang, Pauline Sabinin and Patrick W.K.Lee[1]

Department of Microbiology and Infectious Diseases, University of Calgary Health Sciences Centre, Calgary, Alberta, Canada T2N 4N1

JOURNAL OF VIROLOGY, May 2006, p. 4422–4430 Vol. 80, No. 9
0022-538X/06/$08.00+0 doi:10.1128/JVI.80.9.4422–4430.2006

Negative Regulation of the Alpha Interferon-Induced Antiviral Response by the Ras/Raf/MEK Pathway

Sarah M. Battcock, Thaddeus W. Collier, Dong Zu, and Kensuke Hirasawa*

Division of Basic Medical Sciences, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Canada

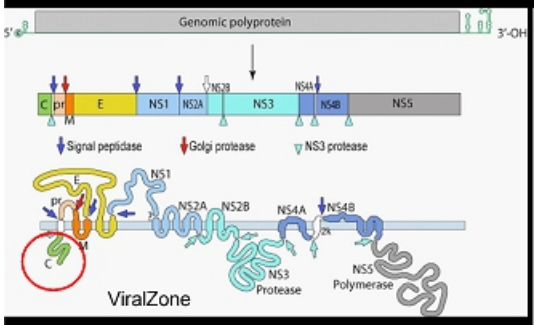
JOURNAL OF VIROLOGY, July 2009, p. 6717–6726 Vol. 83, No. 13
0022-538X/09/$08.00+0 doi:10.1128/JVI.02213-08

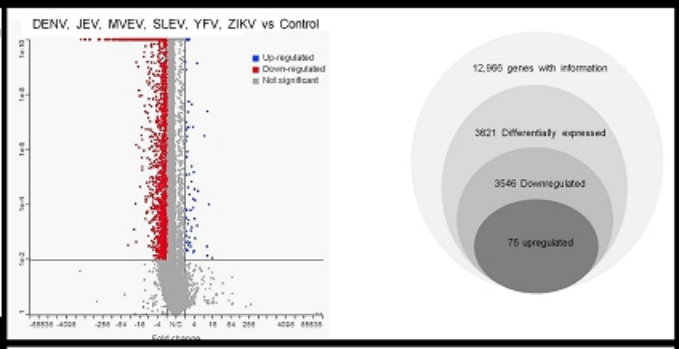
Activated Ras/MEK Inhibits the Antiviral Response of Alpha Interferon by Reducing STAT2 Levels[▽]†

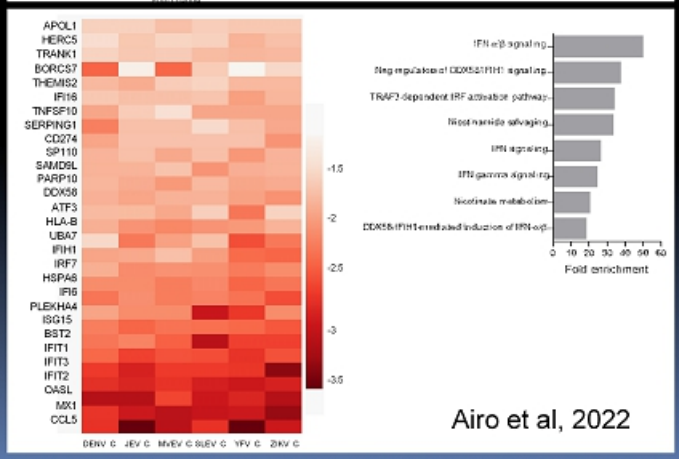
Sherri L. Christian, Thaddeus W. Collier, Dong Zu, Maria Licursi, Chris M. Hough, and Kensuke Hirasawa*

Division of BioMedical Sciences, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Canada

Flavivirus capsids downregulate the IFN response

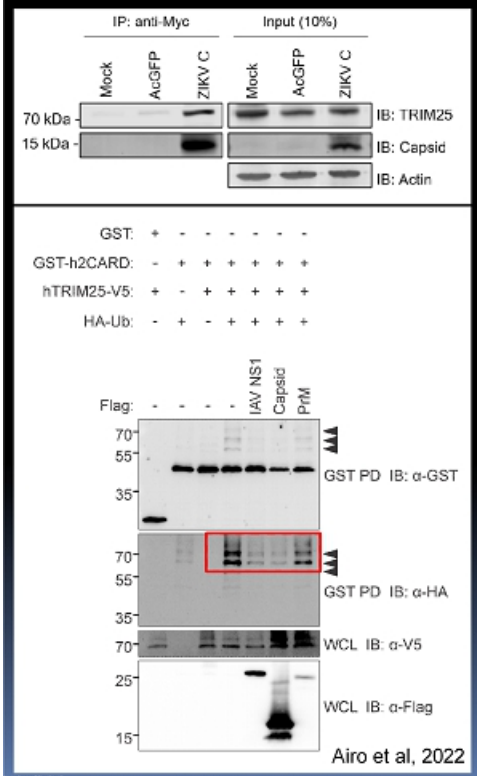




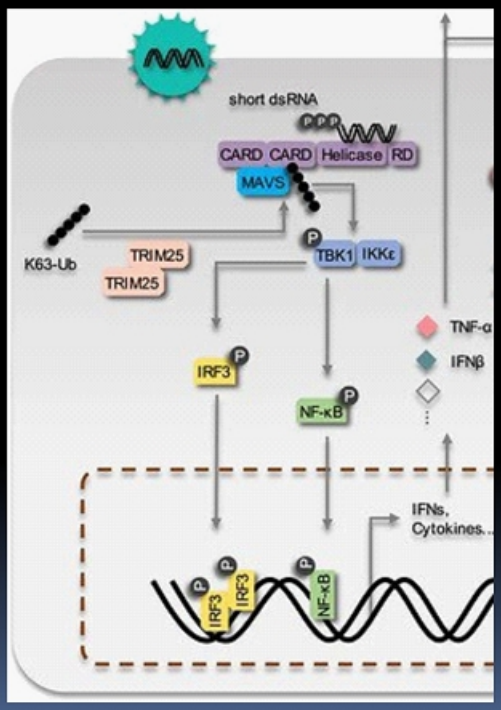


Airo et al, 2022

ZIKV capsid inhibits RIG-I ubiquitination by TRIM25



Airo et al, 2022



Yang et al, 2021

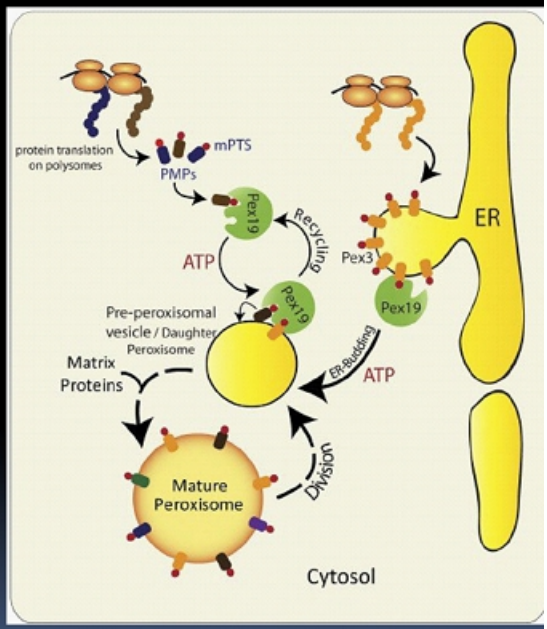
Flaviviruses use many strategies to inhibit IFN response

- Non-structural proteins block IFN induction and signaling by targeting NFκB, IRF3 and STAT2
  - Mechanisms known in many cases
- Upregulated FGF signaling blocks IFN induction and ISG expression
  - MEK-dependent pathway
- Capsid proteins block IFN induction
  - Inhibits TRIM25-mediated activation of RIG-I
    - Conserved mechanism among flaviviruses
  - Occurs before NS proteins act?
- Others?

Conserved interactions between flavivirus capsid proteins and host proteins

	FLAG-DENV				FLAG-WNV				FLAG-UL137			
	Method 1		Method 2		Method 1		Method 2		Method 1		Method 2	
	UP	SC	UP	SC	UP	SC	UP	SC	UP	SC	UP	SC
DENV	1	1	4	17	0	0	0	0	0	0	0	0
WNV	0	0	0	0	1	1	5	6	0	0	0	0
Pex 19	3	4	5	9	5	5	6	8	0	0	0	0

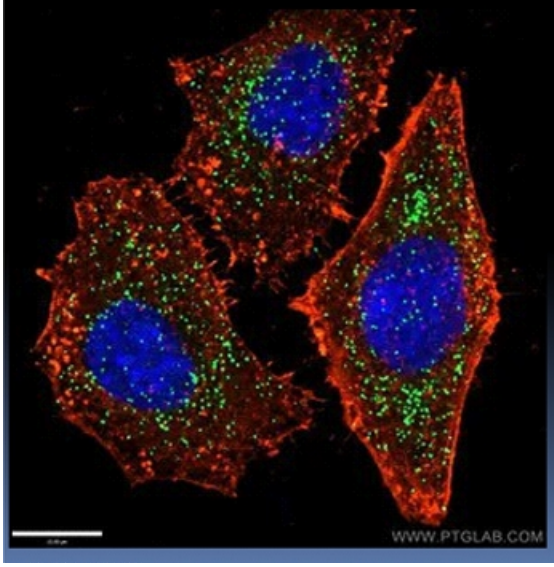
You, Hou et al, 2015

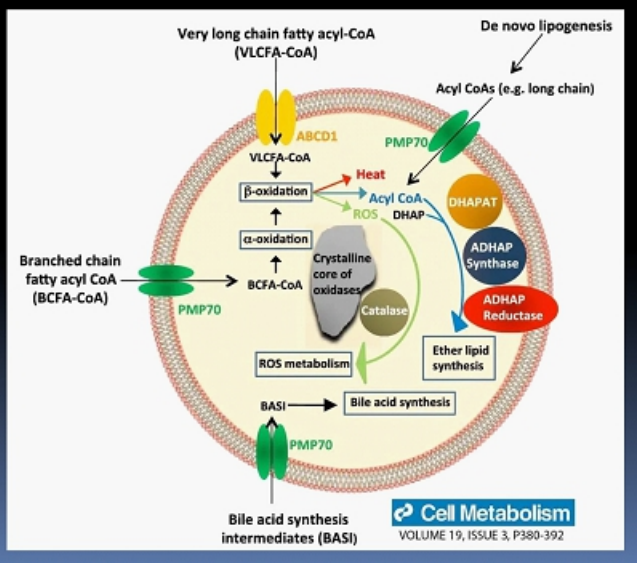


Ma et al, 2011

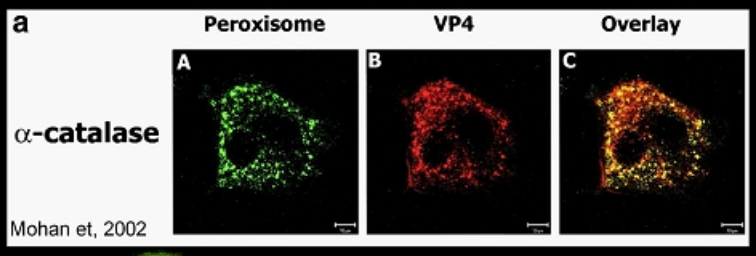
Peroxisomes are membranous organelles that:

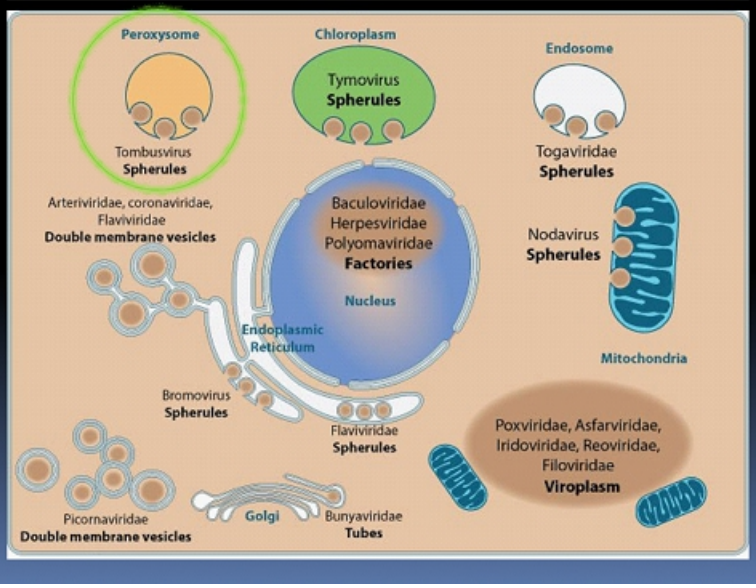
- Catabolize very long chain fatty acids
- Regulate reactive oxygen species
- Are sites of biosynthesis for specialized phospholipids
- Control inflammation





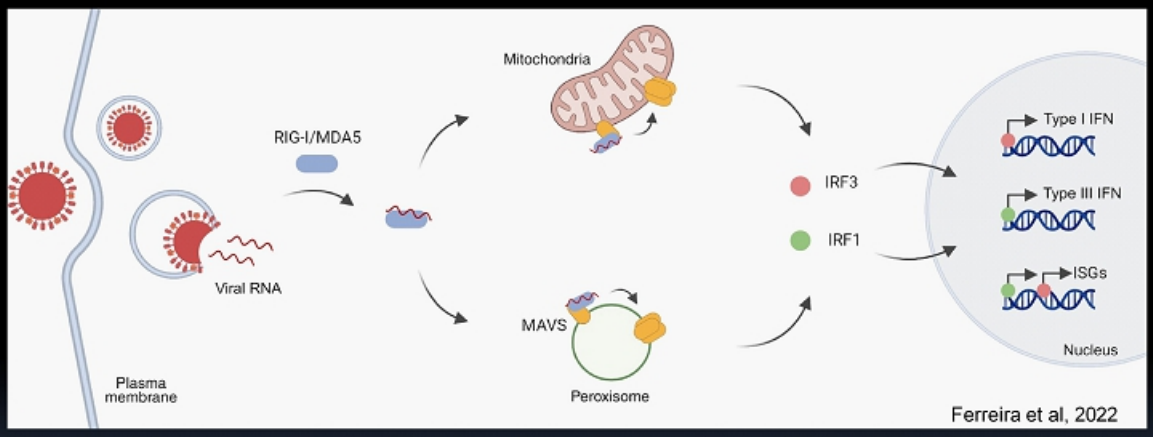
Knowledge gap regarding viruses and peroxisomes





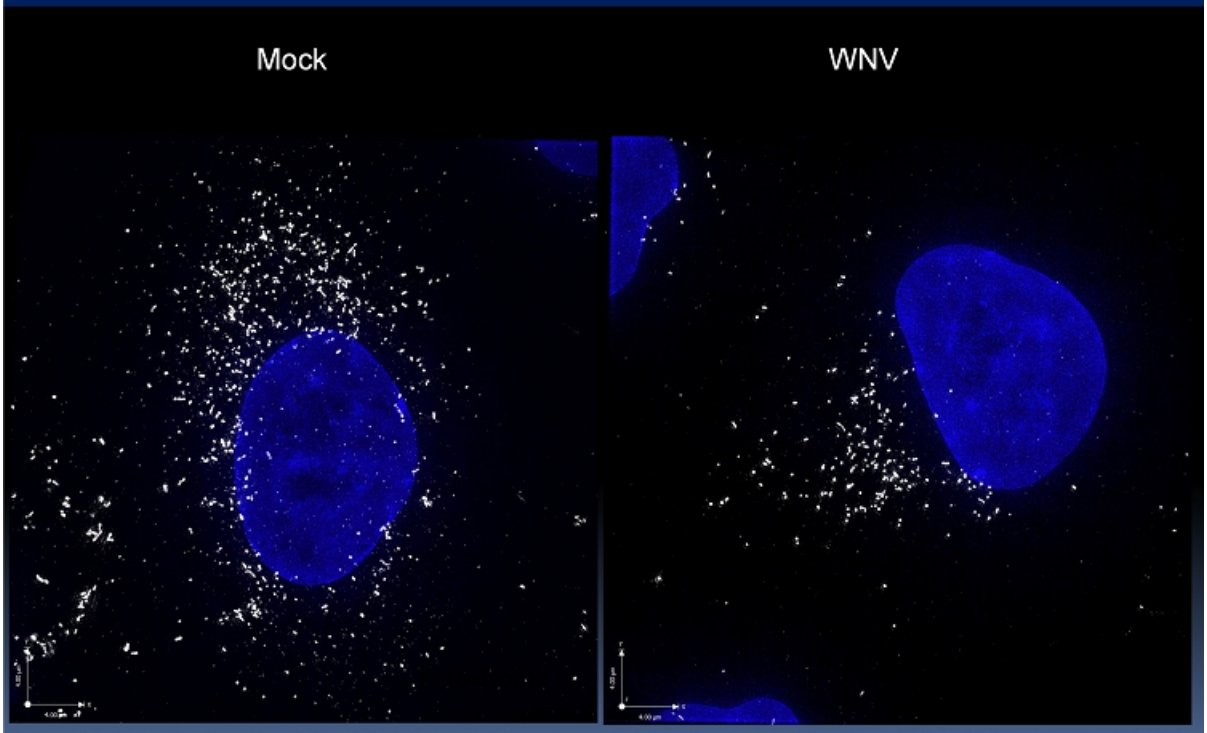
ViralZone

Peroxisomes are Antiviral Signaling Platforms



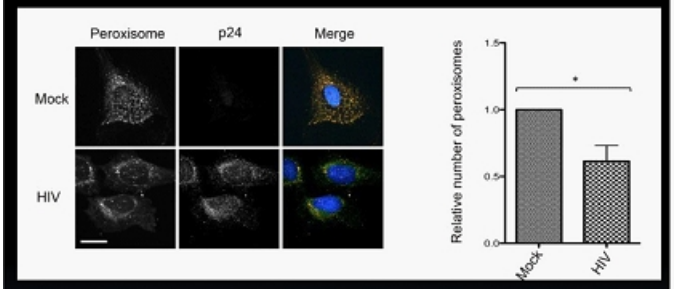
What happens to peroxisomes during viral infection?

Flavivirus infection results in loss of peroxisomes

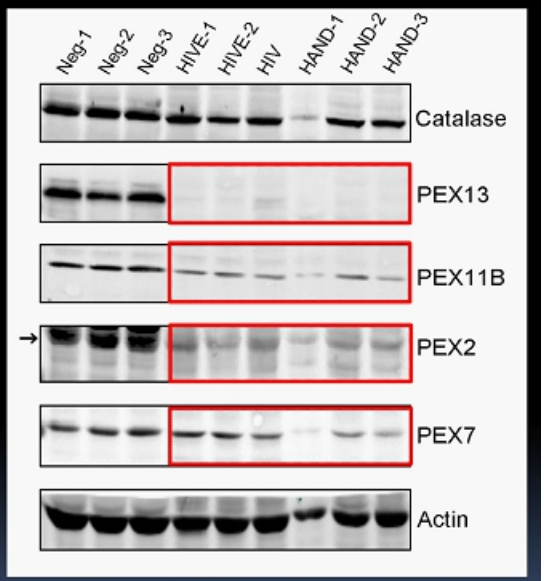


You, Hou *et al*. 2015

HIV-1 infection also depletes peroxisomes



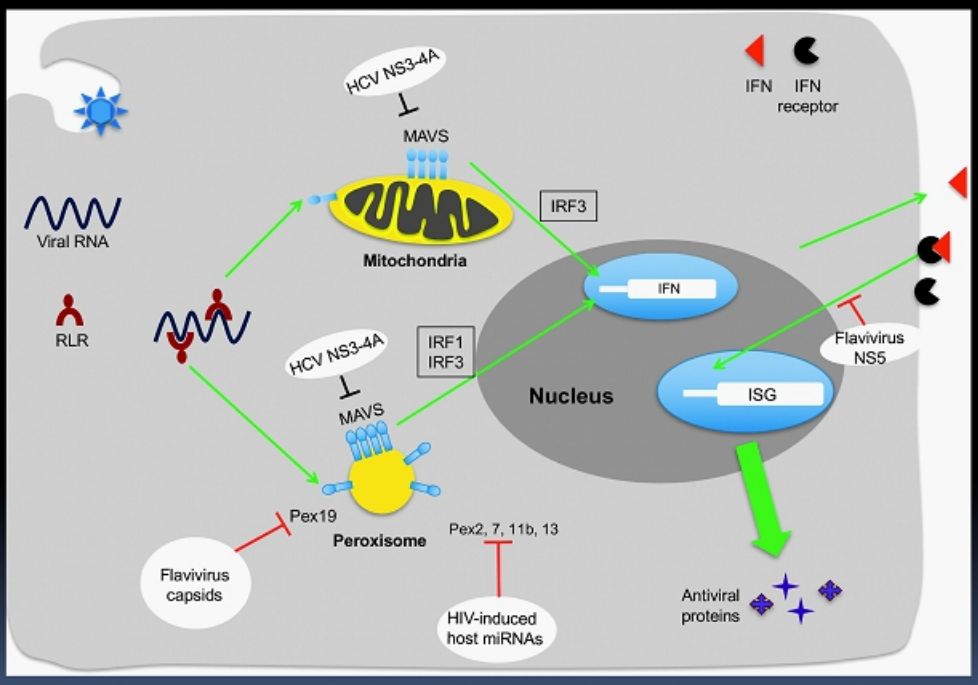
Xu *et al*, 2017



HIVE-HIV with encephalitis

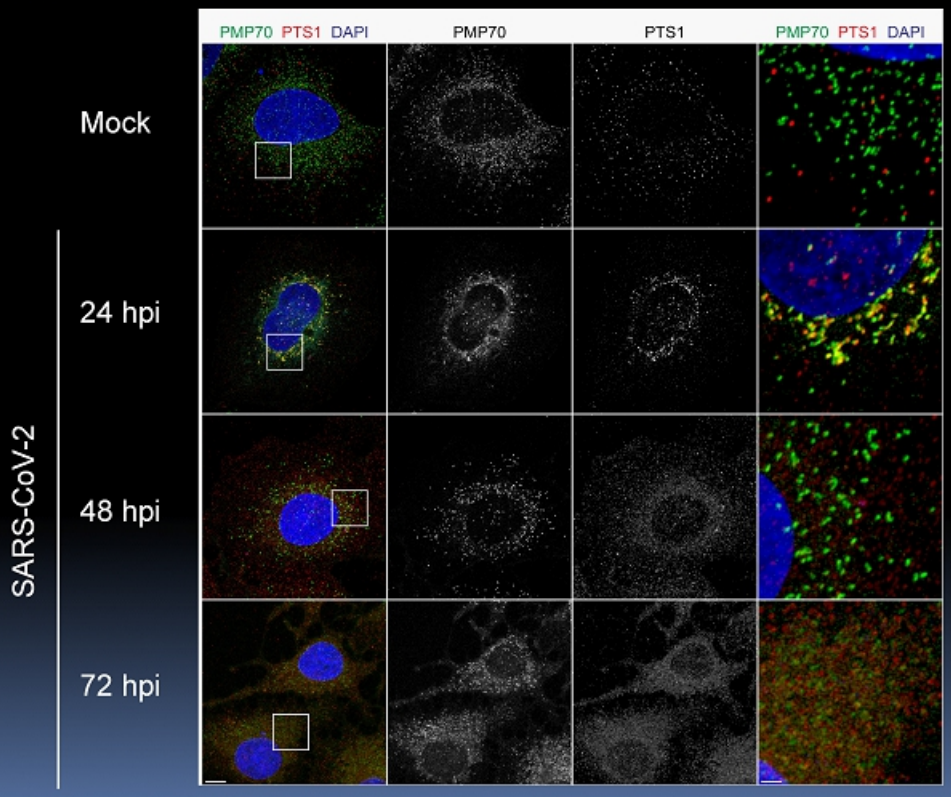
HAND-HIV-Associated Neurocognitive Disorder

Different mechanisms, same result….



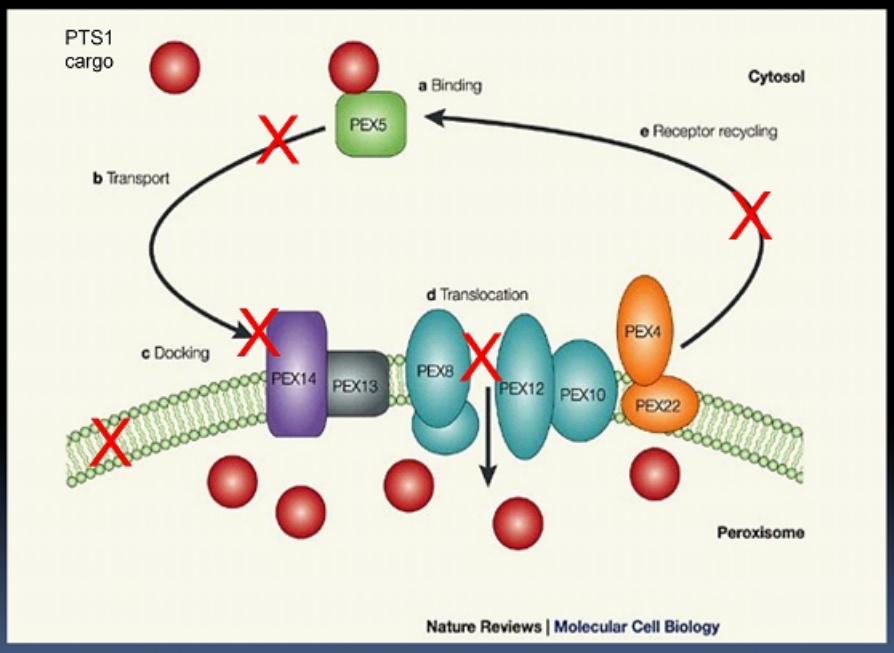
Wong *et al*, 2018

SARS-CoV-2 infection depletes functional peroxisomes

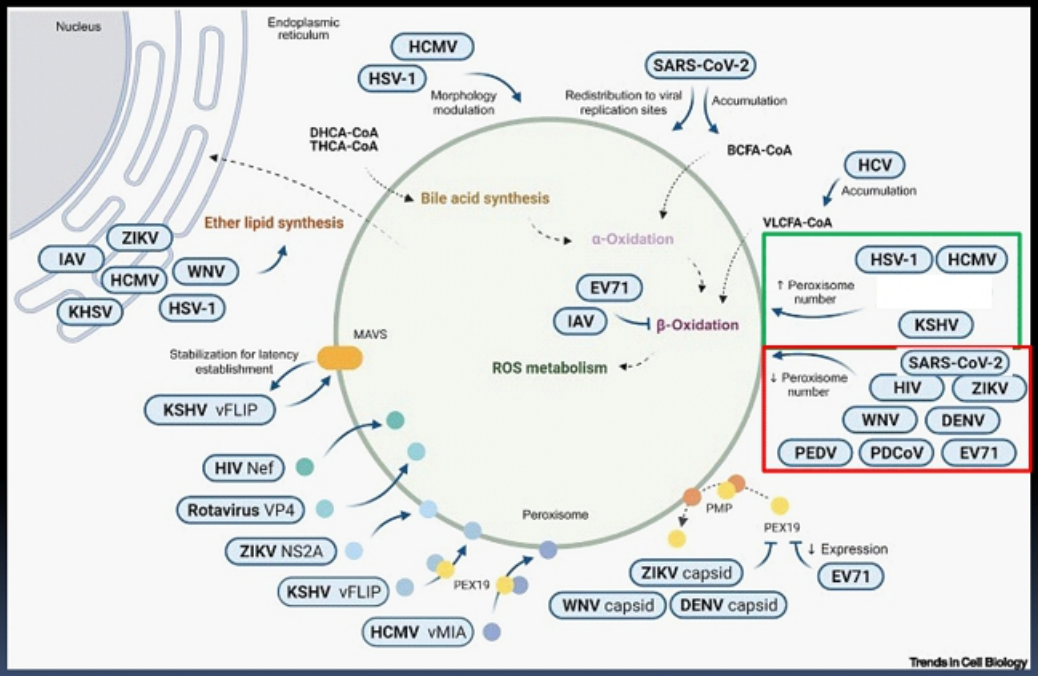


Knoblach et al, 2021

SARS-CoV-2 infection impairs import of matrix proteins

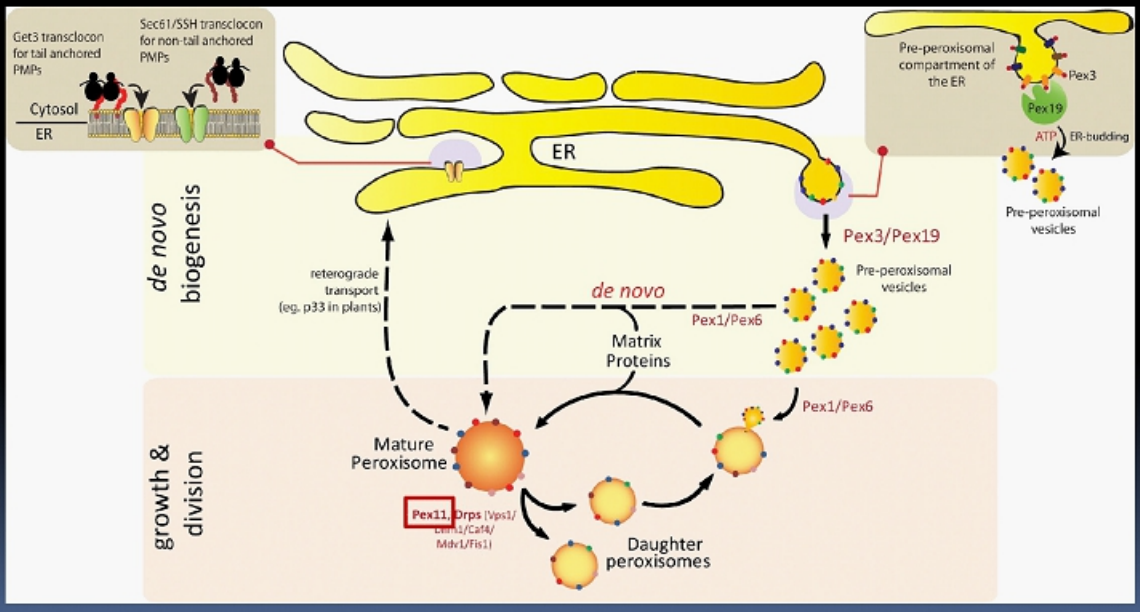


Some viruses upregulate peroxisomes



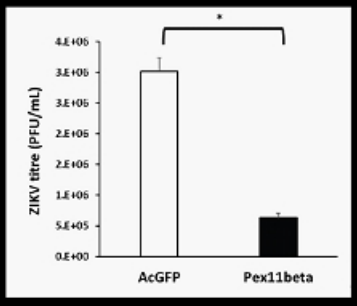
Ferreira et al, 2022

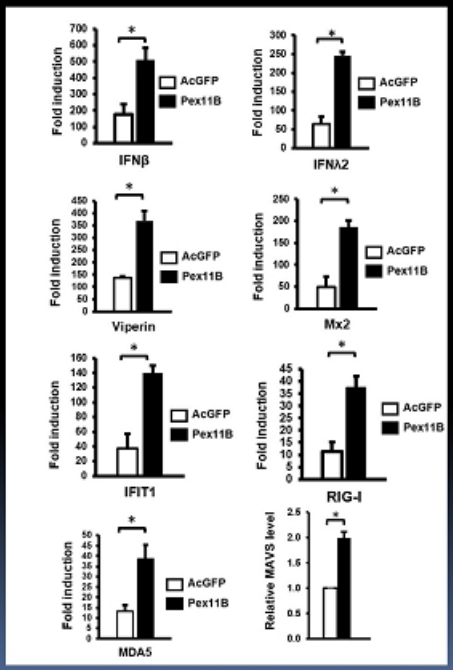
Peroxisomes pool is maintained by 2 main pathways



Ma et al, 2011

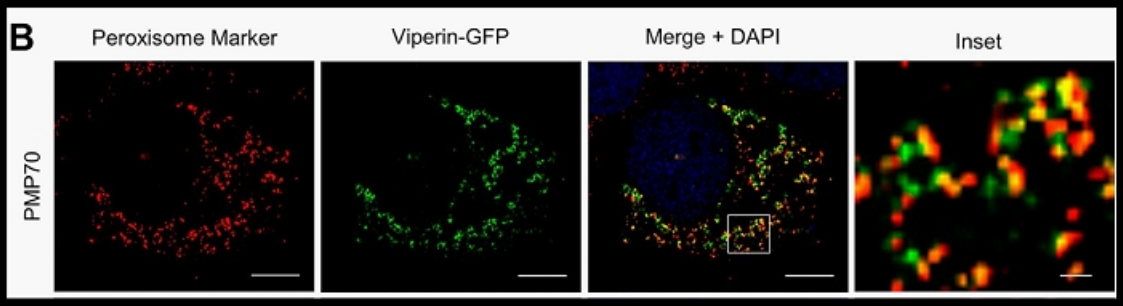
Genetic induction of peroxisomes by Pex11 inhibits ZIKV replication by enhancing IFN response





Wong et al, 2019

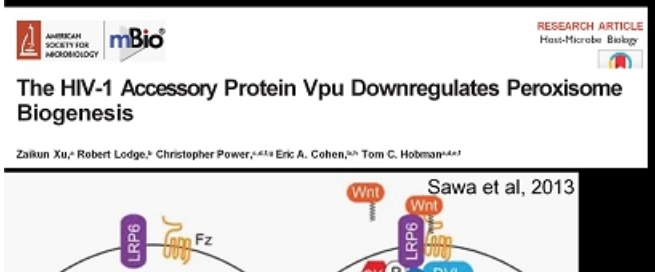
The ISG Viperin associates with peroxisomes



Khantisitthiporn et al, 2021

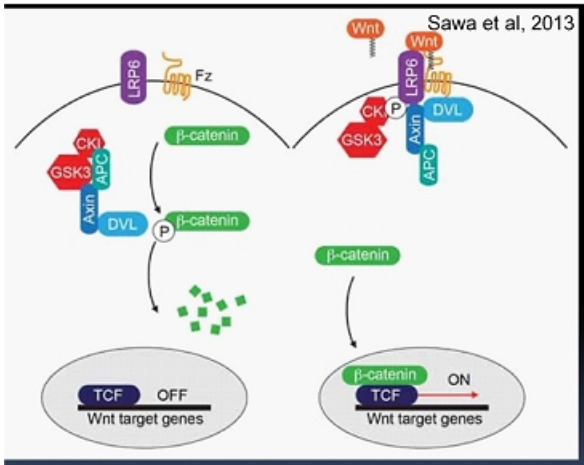
- Potentiates the innate antiviral response
- Positive feedback mechanism?
- Positioning peroxisomes near the mitochondrial/MAM MAVS signaling synapse?

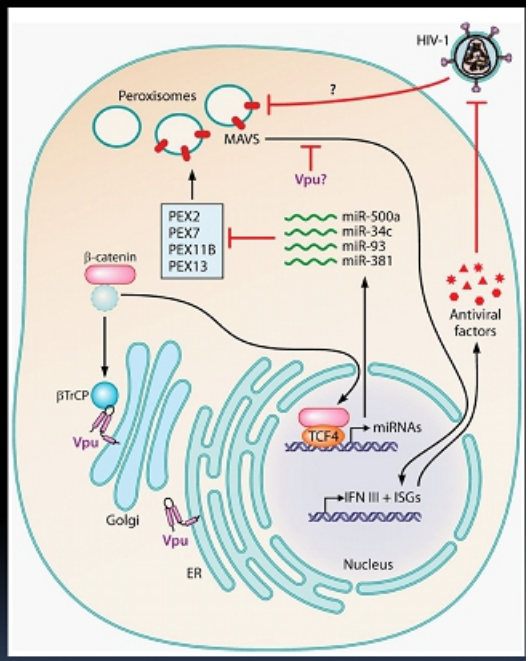
The power and serendipity of collaboration……


mBio®
RESEARCH ARTICLE
Host-Microbe Biology

The HIV-1 Accessory Protein Vpu Downregulates Peroxisome Biogenesis

Zaikun Xu,[a] Robert Lodge,[b] Christopher Power,[a,c,d,e] Eric A. Cohen,[b,h] Tom C. Hobman[a,d,e,f]

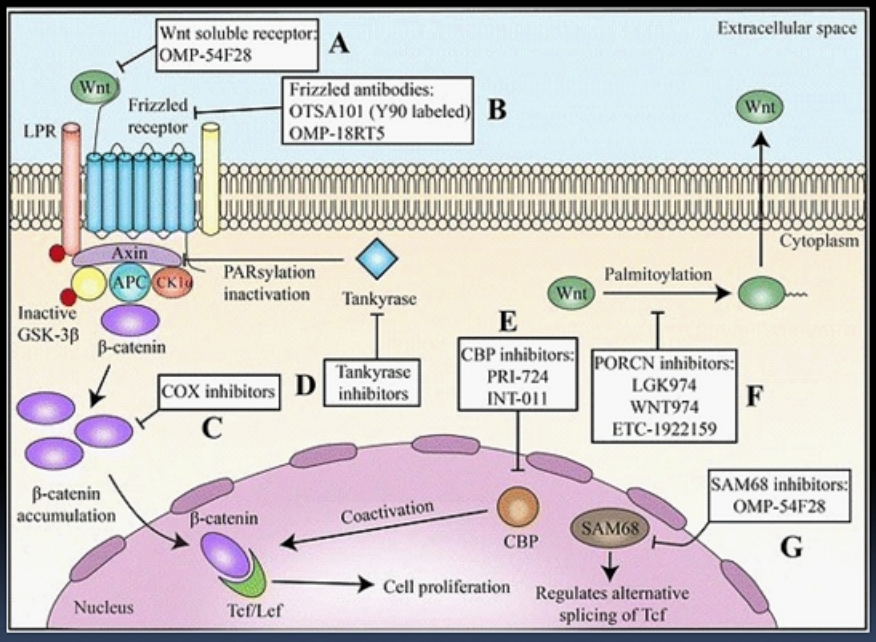




Hopfensperger et al, 2020

So what?

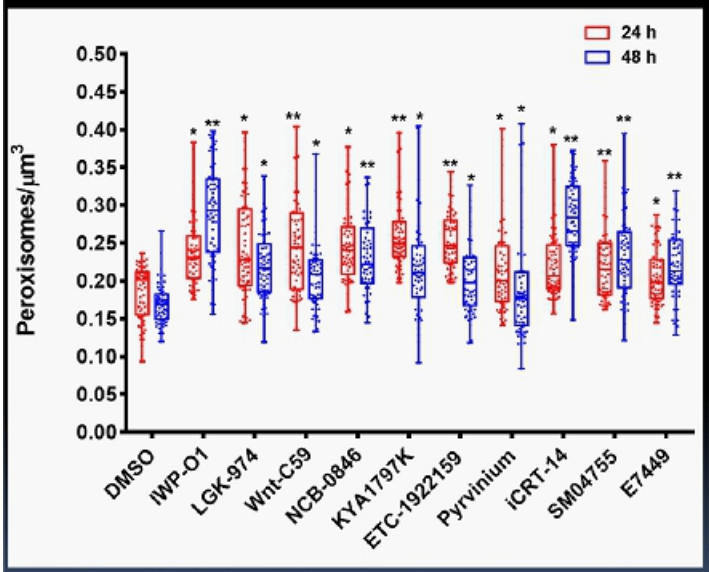
Lots of drugs that inhibit Wnt signaling pathway

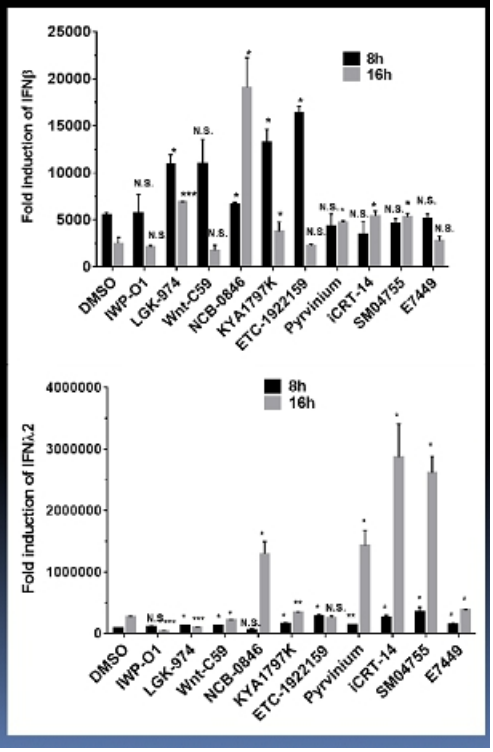


Pai et al, 2017

Do these types of drugs induce peroxisomes??

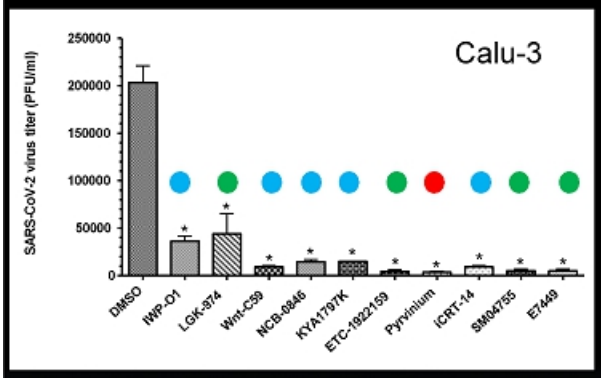
Wnt/β-catenin inhibitors increase peroxisome density and potentiate the IFN response during viral infection

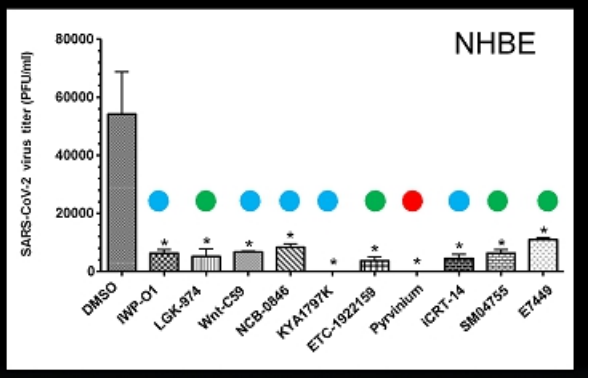




Xu, Wong et al, in preparation

Wnt/β-catenin inhibitors inhibit SARS-CoV-2 replication in multiple cell types



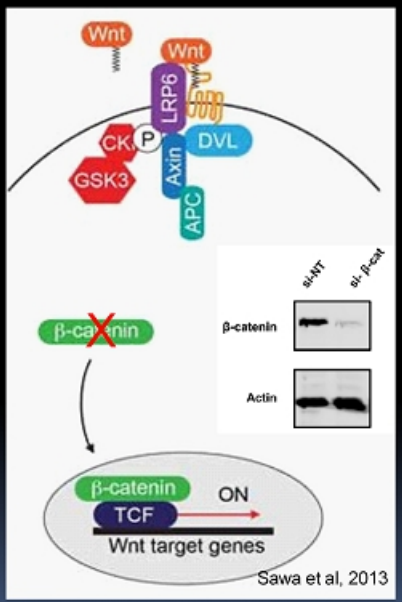


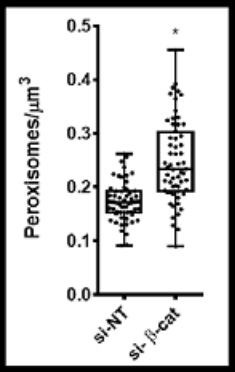
Xu, Wong et al, in preparation

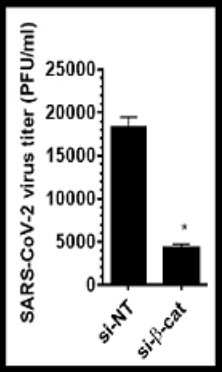
- Licensed for human use
- Phase I or II
- Preclinical

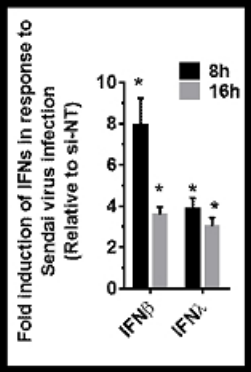
- No effect in Vero cells
- IFN requirement?

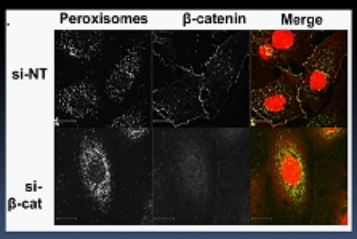
Reducing β-catenin levels induces peroxisome proliferation and enhances IFN response

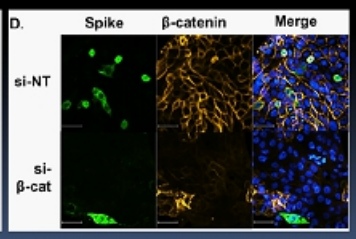






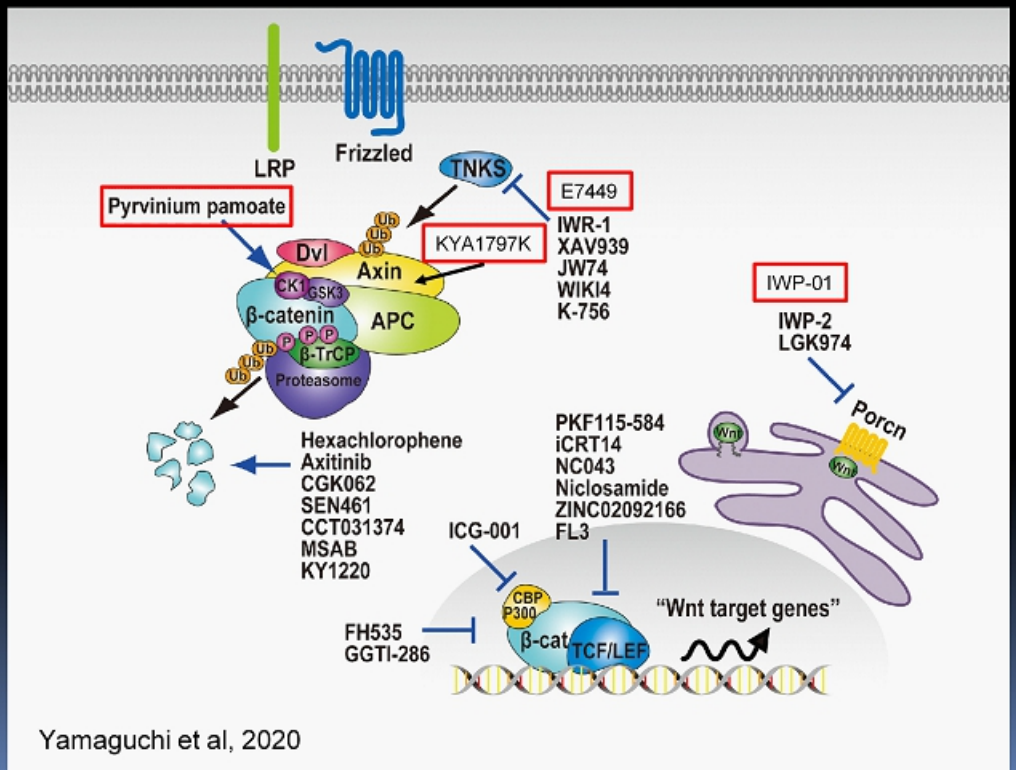






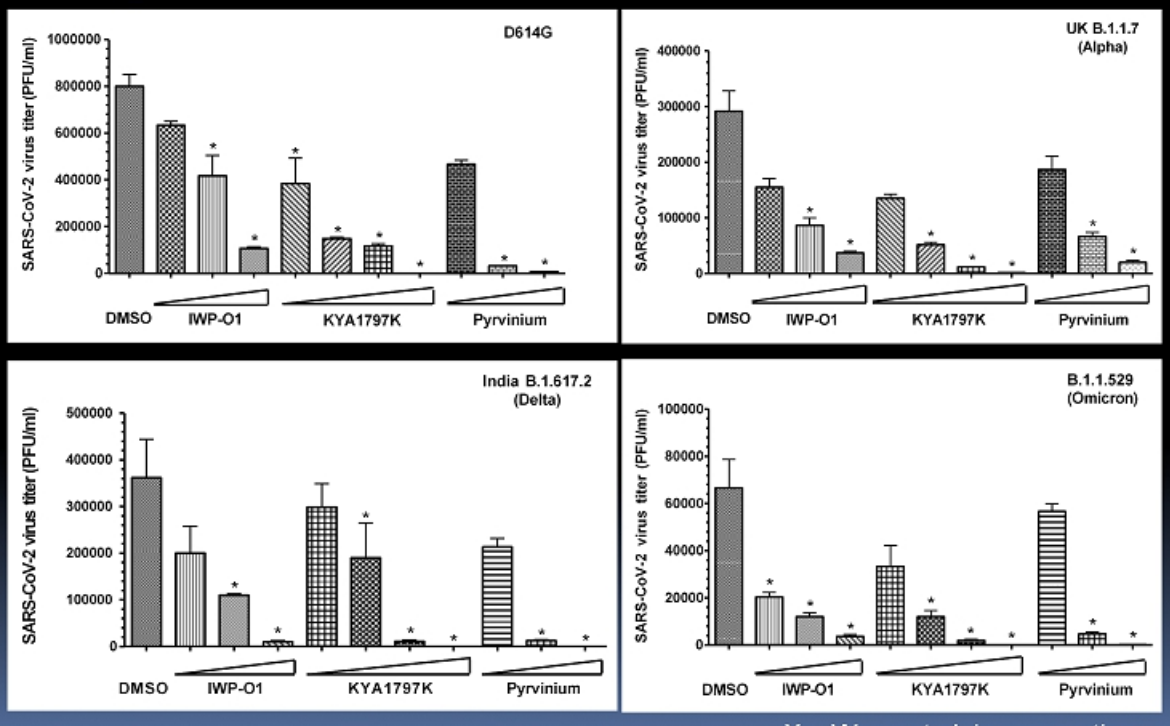
Xu, Wong et al, in preparation

Drugs with high SIs chosen for testing against Variants of Concern and small animal studies



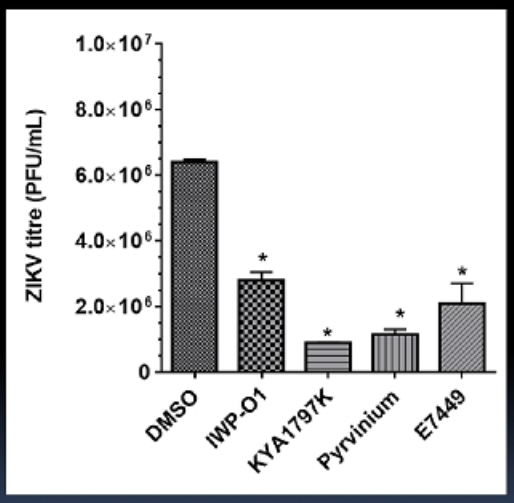
Yamaguchi et al, 2020

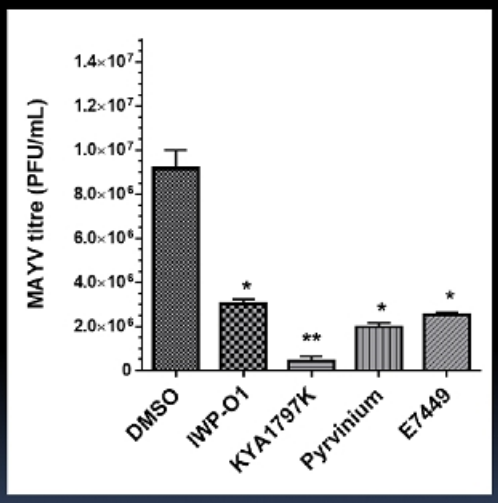
Peroxisome-modulating drugs are effective against SARS-CoV-2 Variants of Concern



Xu, Wong et al, in preparation

Peroxisome-inducing drugs reduce replication of other RNA viruses



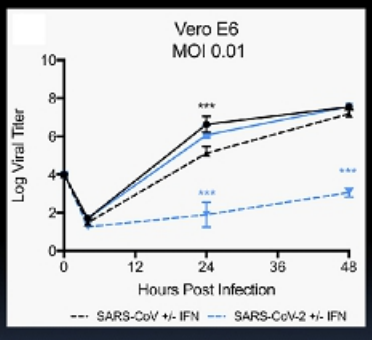


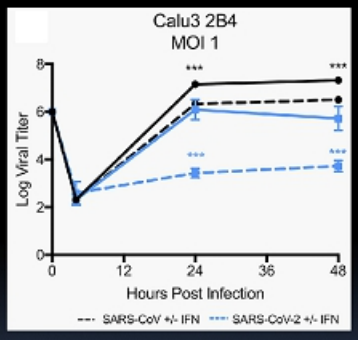
Xu, Wong et al, in preparation

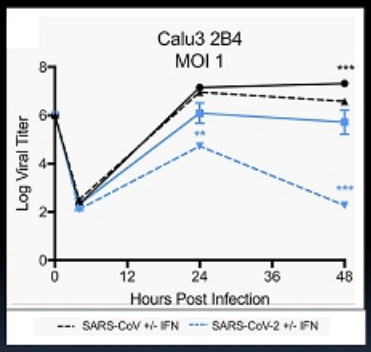
SARS-CoV-2 is highly sensitive to Interferon

IFN added pre-infection

IFN added post-infection



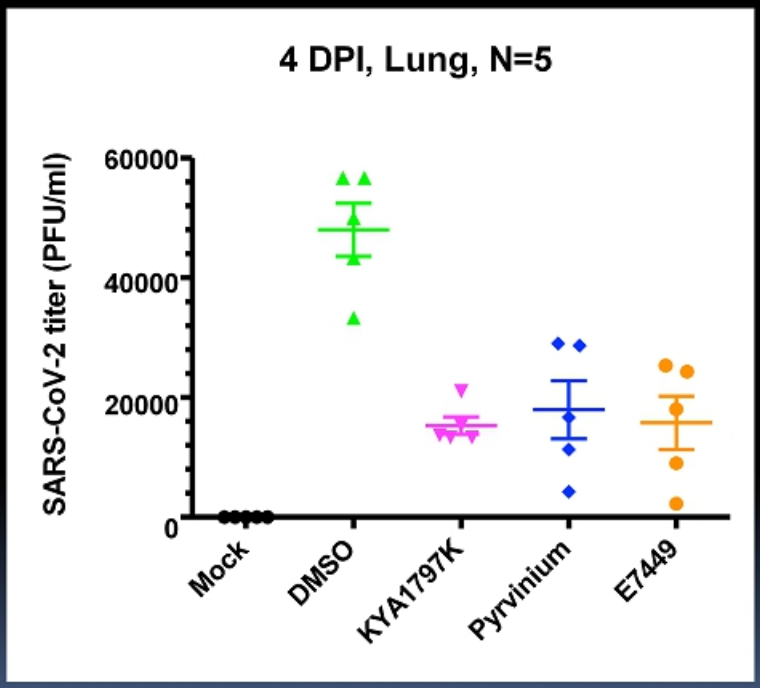




Lokugamage *et al*, 2020

In vivo testing of Wnt inhibitors

Promising trend……



- Mice infected with $10x^3$ pfu of mouse-adapted SARS-CoV-2
- Drugs administered IP pre- and post-infection

Summary

- RNA viruses employ a highly diverse array of tactics to block innate immune signaling
- This includes novel mechanisms to disrupt biogenesis and/or function of peroxisomes during infection
- Wnt signaling plays a role in peroxisome homeostasis
- Genetic or pharmacological upregulation of peroxisomes enhances the IFN response during viral infection

Potential benefits of targeting peroxisomes for antiviral therapy

- Drugs ……..lots of them!
  - Wnt inhibitors
  - Peroxisome proliferator-activated receptor agonists
  - Good safety profiles
  - Bench to bedside route shorter
- Broad-spectrum antiviral activity
- Reduce inflammation?
- Prophylactic and early therapeutic use?

Ongoing studies and future directions

- Determine how SARS-CoV-2 depletes peroxisomes
  - Candidate viral proteins and interactome studies
- *In vivo* studies
  - Intranasal and oral delivery routes
- Testing antiviral activity of Wnt inhibitors in combination with other drugs
- Screening libraries for additional peroxisome-inducing compounds/drugs
- Metabolic consequences of peroxisome loss?
  - Inflammation and lipotoxicity

Acknowledgements