BLOOD CANCER CARE & COVID-19

YOUR QUESTIONS ANSWERED

WELCOME!

The program will begin shortly.

LEUKEMIA & LYMPHOMA SOCIETY®

Moderator:

Gwen Nichols, MD
Chief Medical Officer | The Leukemia & Lymphoma Society

Featured Presenters:

Catriona Jamieson, MD, PhD
Deputy Director | UCSD Moores Cancer Center

Derrick Rossi, PhD
Chief Executive Officer | Convelo Therapeutics
Co-Founder | Moderna

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OUR PRESENTERS

Catriona Jamieson, MD, PhD
Deputy Director | UCSD Moores Cancer Center

Derrick Rossi, PhD
Chief Executive Officer | Convelo Therapeutics
Co-Founder | Moderna

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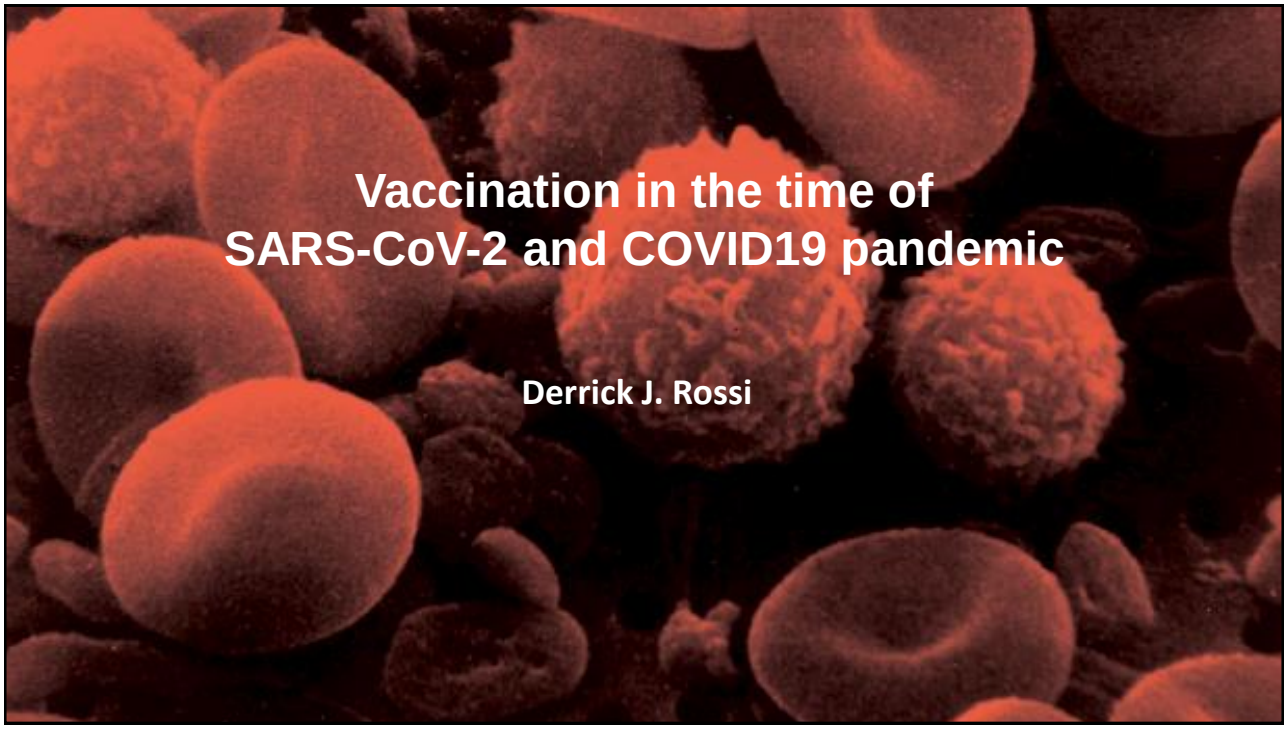

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State of the pandemic

- Respiratory disease breaks out in Wuhan China in late 2019
- First reported case in US on January 15, 2020
- WHO declares outbreak is a global pandemic on March 11, 2020
- Globally, over 2.8 million people have died from COVID19
- In US, 30.8 million people have been infected and >555,000 have died

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What your immune system normally does?

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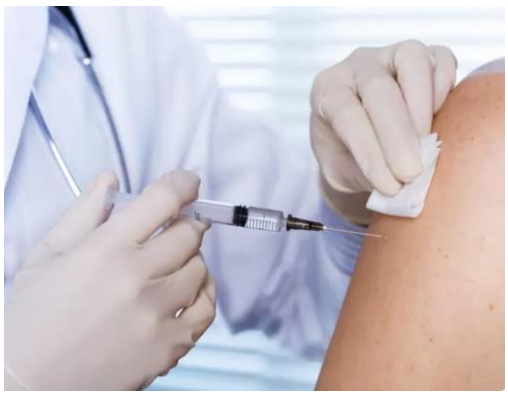
5

What are vaccines and what do they do?

The purpose of vaccines is the introduction of a part of the virus into our bodies so that it will be recognized as *non-self* by our immune systems .



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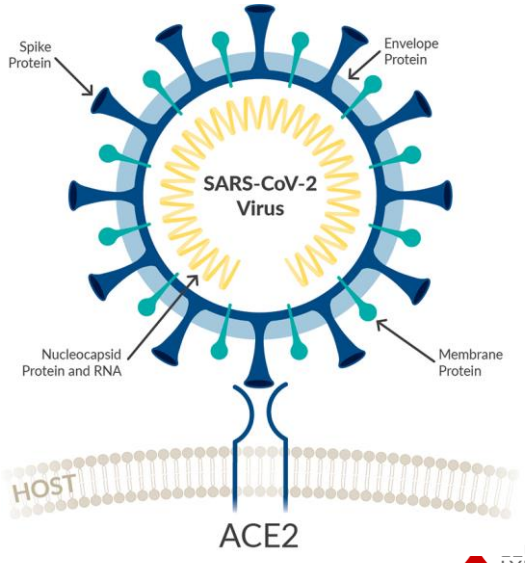
SARs-CoV-2 spike protein

Corona viruses use a protein called the spike protein to initiate their infectious cycle.



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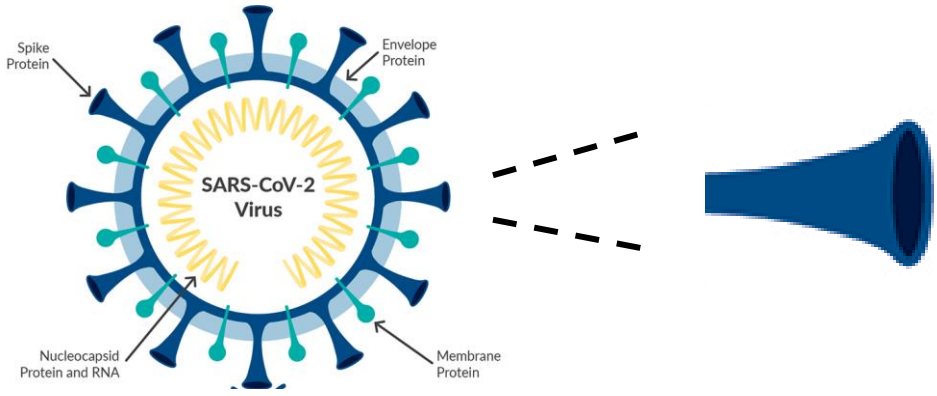
What are vaccines and what do they do?

For vaccines targeting SARS-CoV-2, the vaccines carry instructions to express/introduce the spike protein in our bodies



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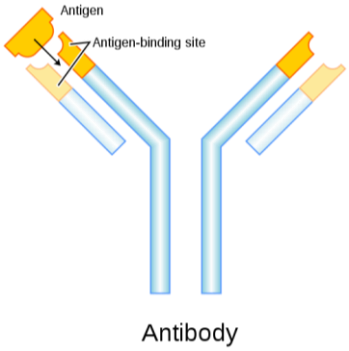
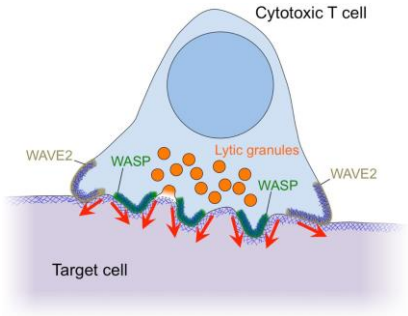
What are vaccines and what do they do?

The immune system of a vaccinated person responds by producing neutralizing antibodies that specifically recognize and bind to the spike protein, and specialized T-cells that mediate cellular immune responses.





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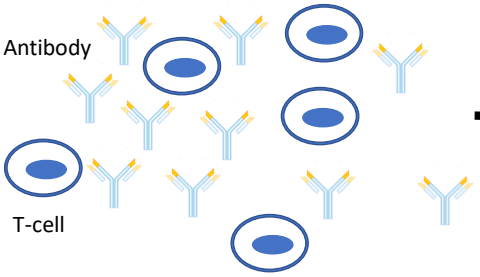
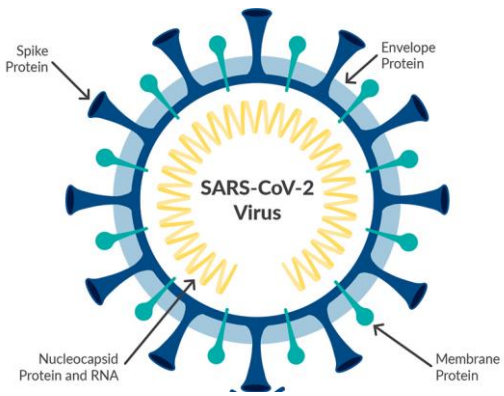
What are vaccines and what do they do?

When a vaccinated person encounters the virus, their immune systems are primed to act quickly blocking the ability of the virus to infect cells (neutralizing antibodies) or killing cells that do become infected (T-cell response).





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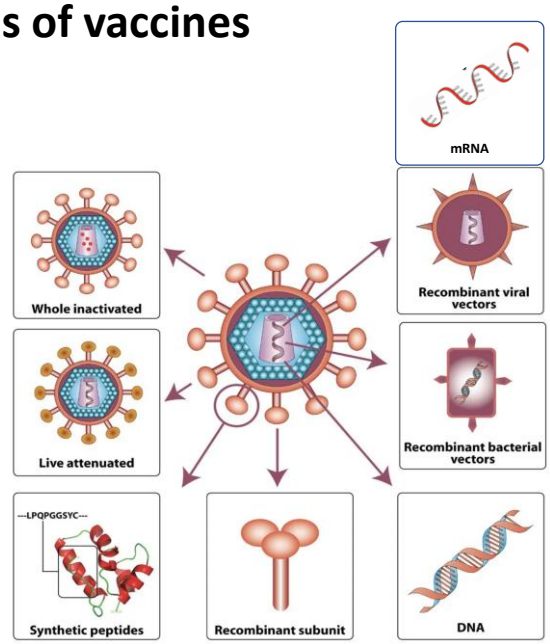
Different types of vaccines

Vaccines developed by Sinopharm, Sinovac

Vaccine developed by Novavax



Vaccines developed by Moderna, BioNTech

Vaccines developed by J&J, AZ

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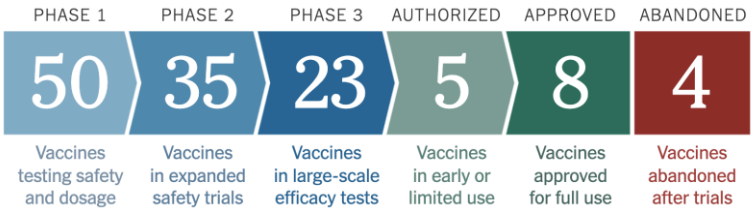
How so fast, transparency



- New technologies, yet extensive clinical experience
- Clinical trial design
- Investment in manufacturing
- Massive mobilization of resource and brain power

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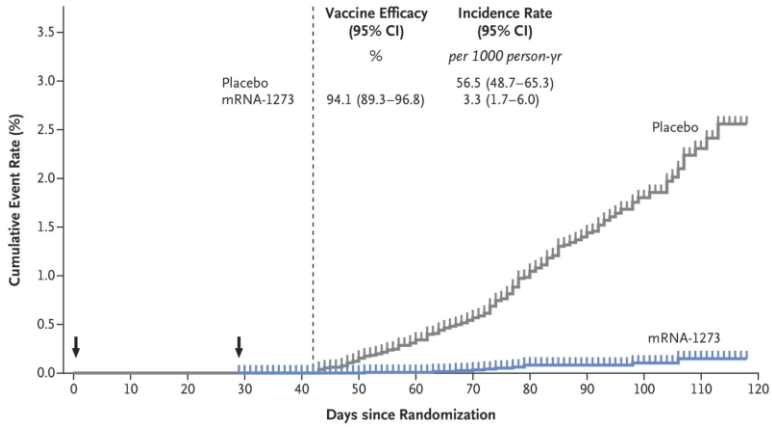
SARS-CoV-2, COVID19 and mRNA-1273

- SAR-CoV-2 genome on web Jan 2020, 42 days later GMP mRNA ready for human trials
- Nov 30, 2020: Phase 3 blinded, placebo-controlled (15,000 vaccine, 15,000 placebo)



NEJM, Dec 2020

- Well tolerated, no serious safety concerns
- 196 cases, 30 severe, 1 death
- 94.1% effective against COVID19, **100% effective against severe disease**

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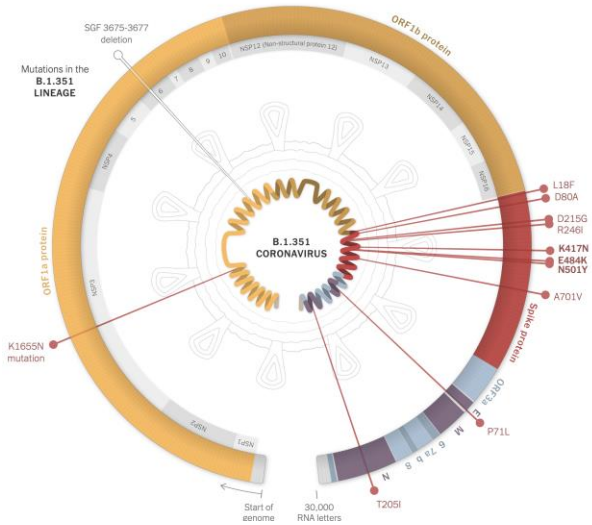
SARS-CoV-2 Variants, mRNA-1273.351



- First identified in South Africa in October 2020 (now 24+ countries)

- Evidence of increased transmissibility

- Vaccine-elicited antibodies were also less effective at neutralizing this variant *in vitro* (trials run in SA show reduced efficacy)

- mRNA-1273-351 shipped to NIH Feb 24th for clinical study

- First patient dosed March 10, 2021

- B1.1.7 (Britain) and P1 (Brazil) variants more infectious but current vaccines appear effective

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BLOOD CANCER RESEARCH AND TREATMENT IN THE TIME OF COVID
C. JAMIESON, MD PHD
PROFESSOR OF MEDICINE AND KOMAN FAMILY ENDOWED CHAIR IN CANCER RESEARCH
DIRECTOR, SANFORD STEM CELL CLINICAL CENTER
DEPUTY DIRECTOR,
UC SAN DIEGO MOORES CANCER CENTER
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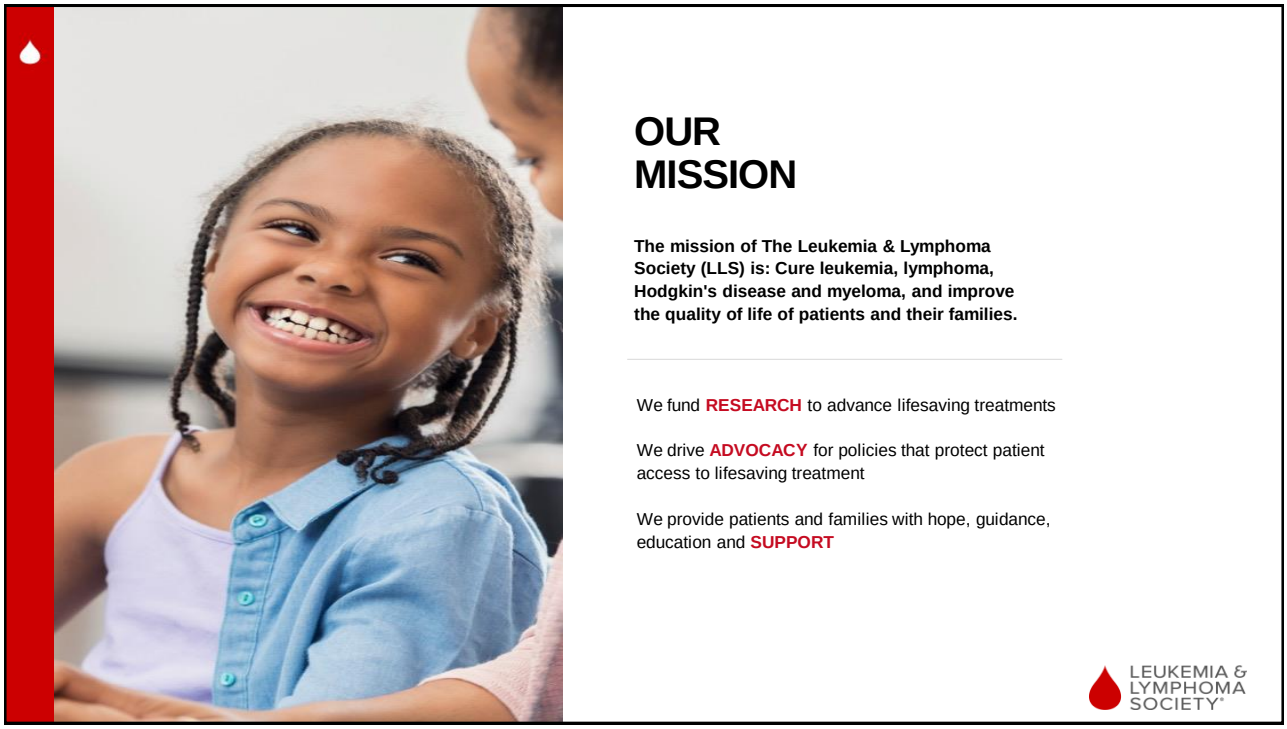
OUR MISSION
The mission of The Leukemia & Lymphoma Society (LLS) is: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.
We fund RESEARCH to advance lifesaving treatments
We drive ADVOCACY for policies that protect patient access to lifesaving treatment
We provide patients and families with hope, guidance, education and SUPPORT
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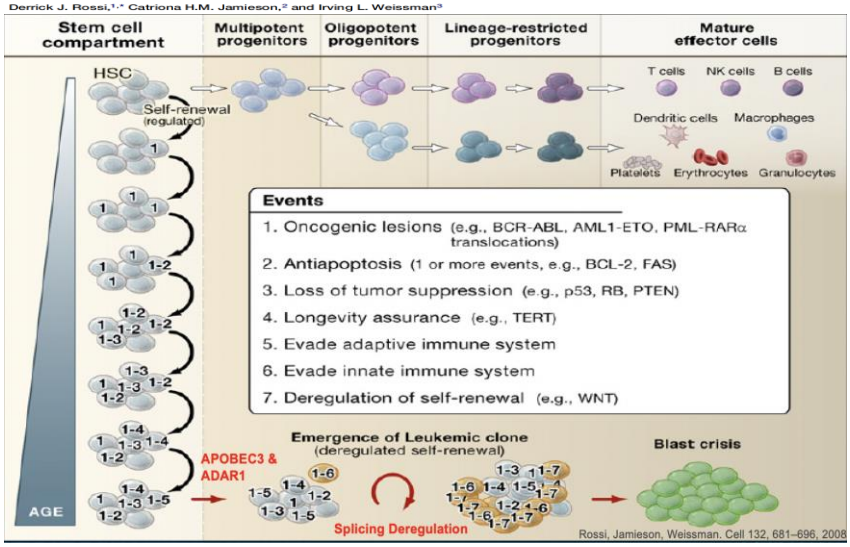
Leading Edge
Review

Cell

Stems Cells and the Pathways to Aging and Cancer

Derrick J. Rossi,[1,*] Catriona H.M. Jamieson,[2] and Irving L. Weissman[3]



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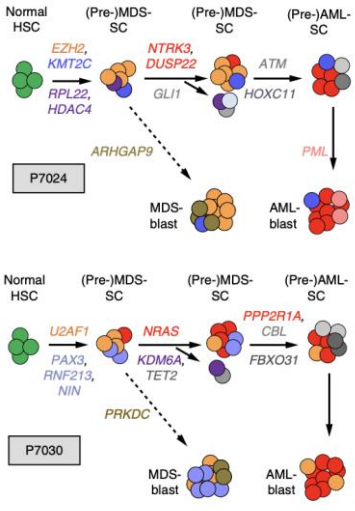
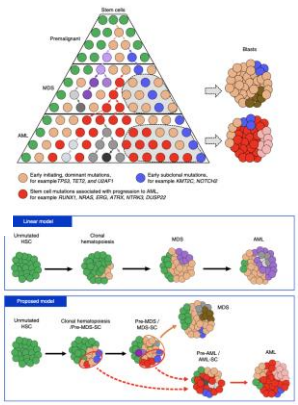
EVOLUTION OF PRE-LEUKEMIA STEM CELLS IN MYELODYSPLASTIC SYNDROME



nature medicine
LETTERS
https://doi.org/10.1038/s41591-018-0267-4
Corrected: Publisher Correction

Myelodysplastic syndrome progression to acute myeloid leukemia at the stem cell level

Jiahao Chen[1], Yun-Ruei Kao[1], Daqian Sun[2,3], Tihomira I. Todorova[1], David Reynolds[4], Swathi-Rao Narayanagari[2,3], Cristina Montagna[5,6], Britta Will[1,2,7,8], Amit Verma[2,7,8,9*] and Ulrich Steidl[1,2,7,8*]



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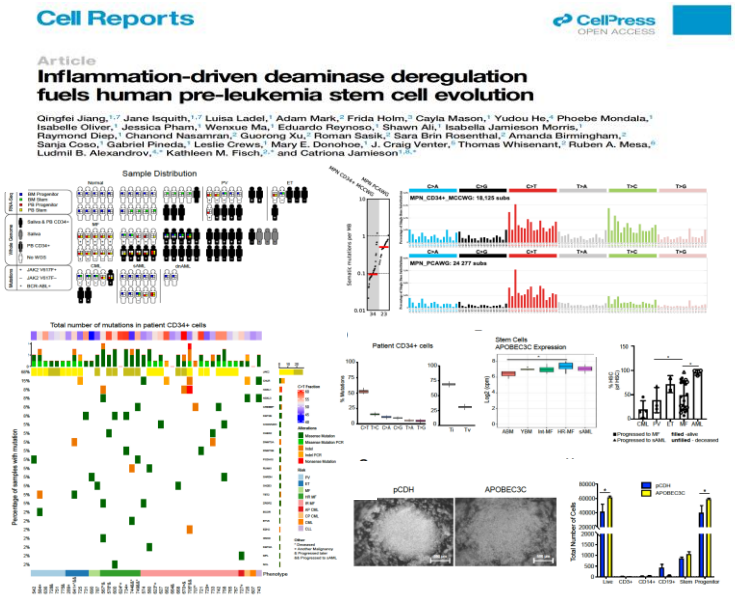
EVOLUTION OF PRE-LEUKEMIA STEM CELLS IN MYELOPROLIFERATIVE NEOPLASMS



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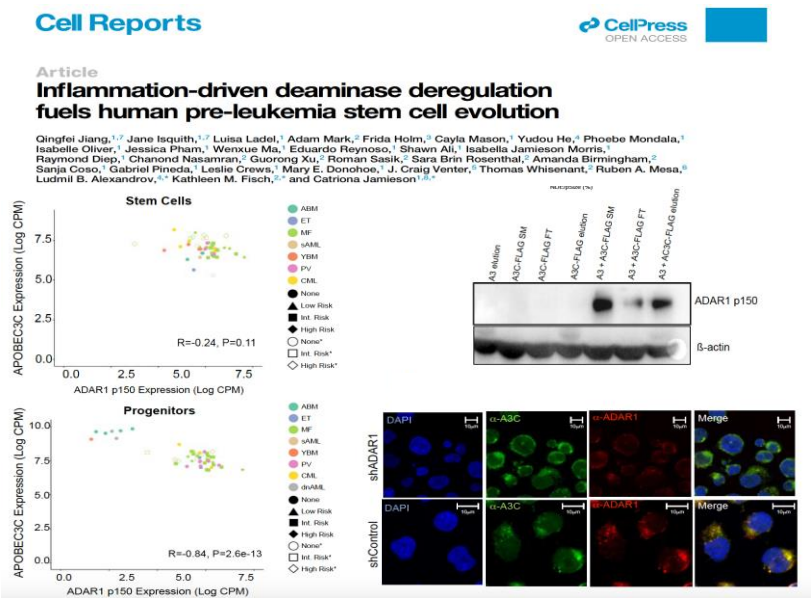
ANTI-VIRAL ENZYME DRIVEN PRE-LEUKEMIA STEM CELL TRANSFORMATION INTO LEUKEMIA STEM CELLS



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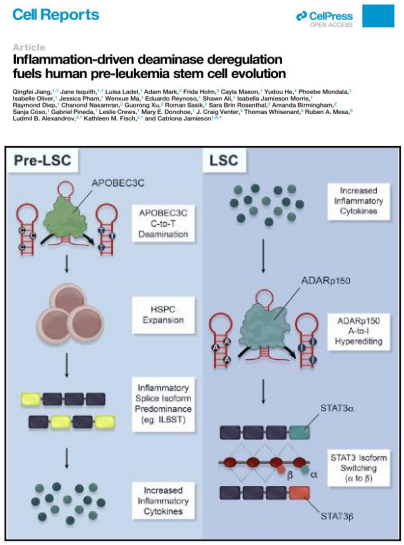
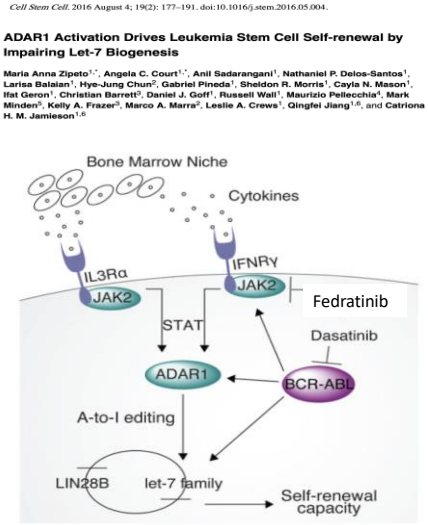
JAK2 INHIBITION REDUCES LEUKEMIA STEM CELL SELF-RENEWAL





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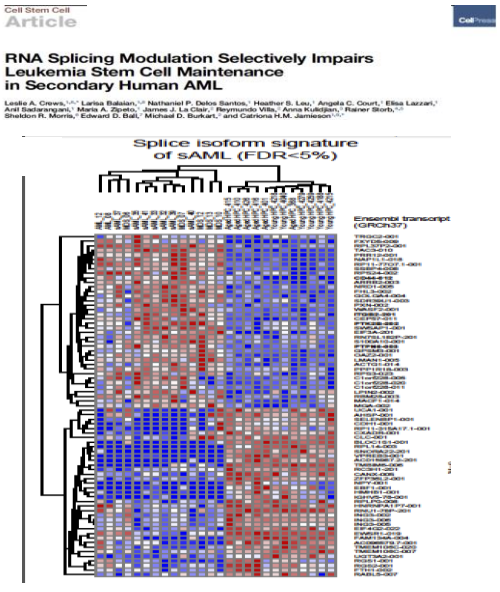
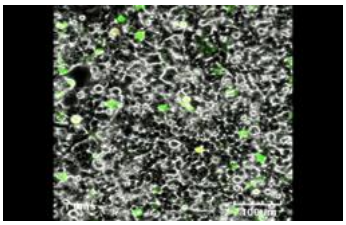
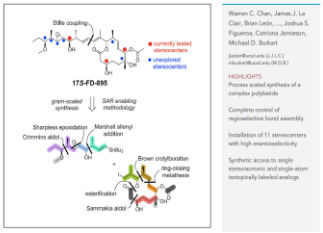
LEUKEMIA STEM CELL TARGETING WITH A SPLICING MODULATOR, REBECSINIB (17S-FD-895)







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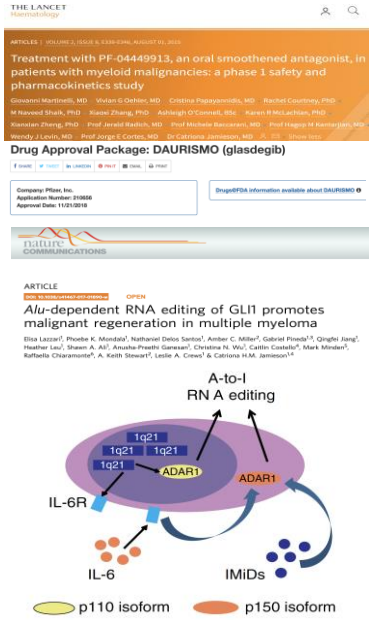
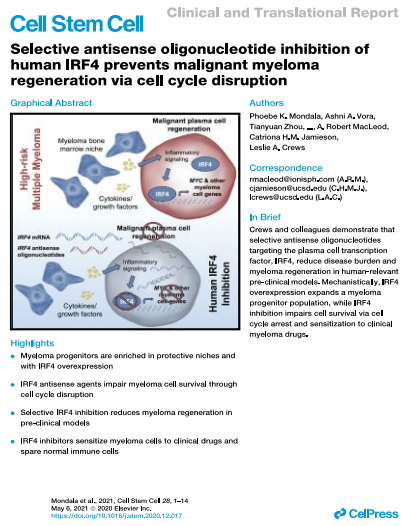
DETECTION AND PREVENTION OF MALIGNANT MYELOMA REGENERATION





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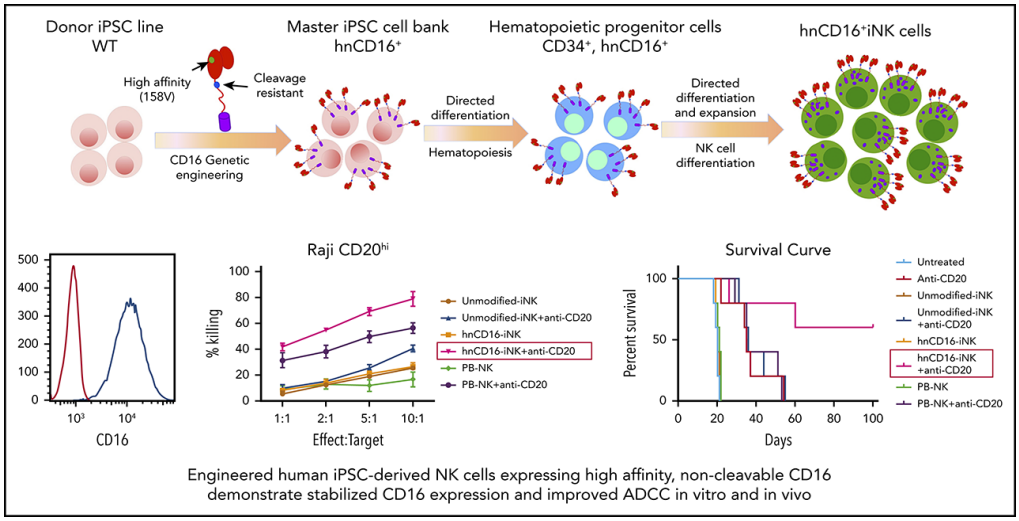
INDUCED PLURIPOTENT STEM CELL DERIVED NK CELL TARGETING OF CANCER



Huang Zhu, Robert H. Blum,… and Dan S. Kaufman. Pluripotent stem cell–derived NK cells with high-affinity non-cleavable CD16a mediate improved antitumor activity. *Blood* (2020) 135 (6): 399.

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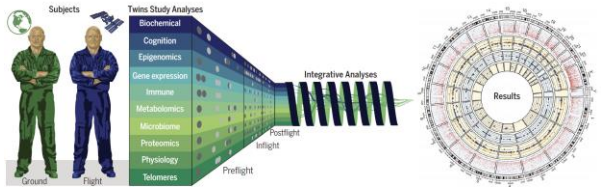
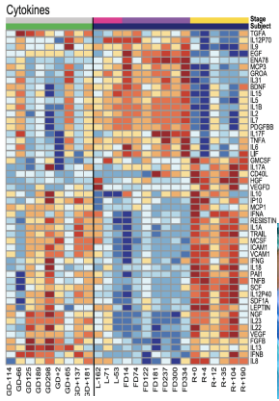
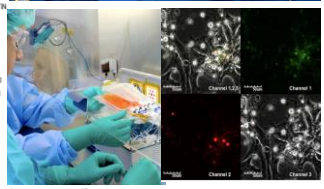
PRE-LEUKEMIA STEM CELL DETECTION IN THE UCSD NASA INTEGRATED SPACE STEM CELL ORBITAL RESEARCH (ISSCOR) LAB

The NASA twin study demonstrated that repeated or protracted periods in low earth orbit (LEO) on the ISS:

- increases inflammatory growth factor expression and may accelerate stem cell aging
- Induces pre-malignant changes in the blood and immune dysfunction
- The **ISSCOR lab** will use stem cell bioreactors and fluorescent reporters of stem cell activity to detect pre-leukemia stem cells







Garrett-Bakelman *et al.*, *Science* **364**, 144 (2019) 12 April 2019

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COVID-19 IN PATIENTS WITH CANCER

Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System

Vikas Mehta[1]*, Sanjay Goel,[2]*, Rafi Kabarriti[3]*, Daniel Cole[2], Mendel Goldfinger[2], Ana Acuna-Villaorduna,[2], Kith Pradhan[2], Raja Thota[4], Stan Reissman[4], Joseph A Sparano[2], Benjamin A. Gartrell,[2], Richard V Smith[1], Nitin Ohri[3], Madhur Garg[3], Andrew D Racine[5], Shalom Kalnicki[3], Roman Perez-Soler[2], Balazs Halmos[2]*, Amit Verma[2]*
* Equal Contribution

Table 2: Disease characteristics of cancer patients with COVID-19 and association with mortality

	Alive	Deceased	P Val
Total	157 (72%)	61 (28%)	
Males	91 (72%)	36 (28%)	0.6
Females	66 (73%)	25 (27%)	0.6
Median Age (Range)	66 (10-92)	76 (10-92)	0.0006
Race			0.602
Caucasian	14 (64%)	8 (36%)	
Hispanic	58 (76%)	18 (24%)	
African American	67(73%)	25 (27%)	
Asian	5 (71%)	2 (29%)	
Other	13 (62%)	8 (38%)	
	N/Total Alive (%)	**N/Total Deceased (%)**	
ICU admission	8 (5%)	15 (24%)	9.10E-05
Ventilator support	10 (6%)	35 (57%)	1.74E-15
Hemodialysis	10 (6%)	6 (10%)	0.37
Metastasis (Solids only)	27 (22%)	15 (37%)	0.06
Active Cancer (<1yr)	60 (38%)	32 (52%)	0.09
Active ChemoTx	34 (22%)	8 (13%)	0.2
Immunotherapy	4 (3%)	1 (2%)	1
Radiation Therapy	38 (24%)	11 (18%)	0.33
DM	53 (34%)	27 (44%)	0.116
HTN	100 (64%)	47 (77%)	0.047
Chronic Lung Dis	34 (22%)	28 (46%)	0.0003
Chronic Kidney Dis	33 (21%)	21 (34%)	0.052
Coronary Artery Dis	24 (15%)	19 (31%)	0.012
CHF	18 (11%)	15 (25%)	0.019

	Alive	Deceased
Total	157 (72%)	61 (28%)
Solid tumors	123(75%)	41 (25%)
Genitourinary	39 (85%)	7 (15%)
Breast	24 (86%)	4 (14%)
Colorectal	13 (62%)	8 (38%)
Gynecologic	8 (62%)	5 (38%)
Lung	5 (45%)	6 (55%)
Head and Neck	7 (88%)	1 (13%)
Neuro	7 (88%)	1 (13%)
Upper GI	5 (63%)	3 (38%)
Hepatobiliary	5 (71%)	2 (29%)
Bone / Soft Tissue	4 (80%)	1 (20%)
Neuro-endocrine	3 (100%)	0 (0%)
Pancreas	1 (33%)	2 (67%)
Skin	2 (67%)	1 (33%)
Hematologic malignancies	34 (63%)	20 (37%)
NHL	10 (67%)	5 (33%)
MDS	2 (40%)	3 (60%)
MPN	5 (71%)	2 (29%)
ALL	4 (100%)	0 (0%)
AML	1 (100%)	0 (0%)
MM	8 (62%)	5 (38%)
CML	0 (0%)	1 (100%)
Hodgkin's	2 (40%)	3 (60%)
CLL	2 (67%)	1 (33%)
Myeloid Malignancy	8 (57%)	6 (43%)
Lymphoid Malignancy	26 (65%)	14 (35%)

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COVID-19 MORTALITY AND IN MYELOPROLIFERATIVE NEOPLASMS

Leukemia (2021) 35:485–493
https://doi.org/10.1038/s41375-020-01107-y

ARTICLE

Chronic Myeloproliferative Neoplasms

High mortality rate in COVID-19 patients with myeloproliferative neoplasms after abrupt withdrawal of ruxolitinib

Tiziano Barbui[1] · Alessandro Maria Vannucchi[2] · Alberto Alvarez-Larran[3] · Alessandra Iurlo[4] · Arianna Masciulli[1] · Alessandra Carobbio[1] · Arianna Ghirardi[1] · Alberto Ferrari[1] · Giuseppe Rossi[5] · Elena Elli[6] · Marcio Miguel Andrade-Campos[7] · Mercedes Gasior Kabat[8] · Jean-Jaques Kiladjian[9] · Francesca Palandri[10] · Giulia Benevolo[11] · Valentin Garcia-Gutierrez[12] · Maria Laura Fox[13] · Maria Angeles Foncillas[14] · Carmen Montoya Morcillo[15] · Elisa Rumi[16] · Santiago Osorio[17] · Petros Papadopoulos[18] · Massimiliano Bonifacio[19] · Keina Susana Quiroz Cervantes[20] · Miguel Sagues Serrano[21] · Gonzalo Carreno-Tarragona[22] · Marta Anna Sobas[23] · Francesca Lunghi[24] · Andrea Patriarca[25] · Begona Navas Elorza[26] · Anna Angona[27] · Elena Magro Mazo[28] · Steffen Koschmieder[29] · Marco Ruggeri[30] · Beatriz Cuevas[31] · Juan Carlos Hernandez-Boluda[32] · Emma Lopez Abadia[33] · Blanca Xicoy Cirici[34] · Paola Guglielmelli[2] · Marta Garrote[3] · Daniele Cattaneo[4] · Rosa Daffini[5] · Fabrizio Cavalca[6] · Beatriz Bellosillo[7] · Lina Benajiba[9] · Natalia Curto-Garcia[35] · Marta Bellini[36] · Silvia Betti[37] · Valerio De Stefano[37] · Claire Harrison[35] · Alessandro Rambaldi[36,38]

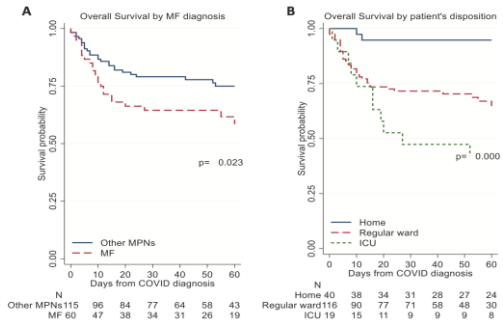

Table 2 Multivariable analysis of risk factors for mortality after COVID-19 diagnosis.

	OR (95% CI)	*p* value
Age	1.07 (1.02–1.11)	0.003
Male sex	2.48 (1.01–6.07)	0.047
MF diagnosis	1.69 (0.61–4.66)	0.315
Chronic heart disease	2.18 (0.64–7.36)	0.210
Respiratory support	10.0 (2.94–34.0)	<0.001
ICU admission	4.93 (1.36–17.9)	0.015
Ruxolitinib administration	2.40 (0.72–8.02)	0.154
Ruxolitinib discontinuation	8.51 (1.14–63.4)	0.037

OR odds ratio, *CI* confidence interval, *MF* myelofibrosis, *ICU* intensive care unit.

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JAK2 INHIBITION OF PRE-LEUKEMIA STEM CELLS AND COVID-19 INDUCED IMMUNE DYSREGULATION

Cancer Cell
Article

Cell PRESS

Selective Inhibition of JAK2-Driven Erythroid Differentiation of Polycythemia Vera Progenitors

Ifat Geron,[1,6] Annelie E. Abrahamsson,[1,6] Charlene F. Barroga,[1] Edward Kavalerchik,[1] Jason Gotlib,[2] John D. Hood,[3] Jeffrey Durocher,[4] Chi Ching Mak,[3] Glenn Noronha,[3] Richard M. Soll,[3] Ayalew Tefferi,[5] Ken Kaushansky,[1] and Cattriona H.M. Jamieson[1,*]

FDA approves fedratinib for myelofibrosis

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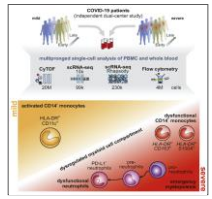
On August 16, 2019, the Food and Drug Administration approved fedratinib (INREBIC, Impact Biomedicines, Inc.) for adults with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

Cell

Article

Severe COVID-19 Is Marked by a Dysregulated Myeloid Cell Compartment

Graphical Abstract



Authors
Jonas Schulte-Schrepping, Nico Reusch, Daniela Paclik, ..., Antonio-Emmanuel Saliba, Leif Erik Sander, Deutsche COVID-19 OMICS Initiative (DeCOI)

Correspondence
j.schultze@uni-bonn.de

In Brief
Analysis of patients with mild and severe COVID-19 reveals the presence of dysfunctional neutrophils in the latter that is linked to emergency myelopoiesis.

Highlights
- SARS-CoV-2 infection induces profound alterations of the myeloid compartment
- Mild COVID-19 is marked by inflammatory *HLA-DR*^{hi}*CD11c*$^{+/-}$ *CD14*$^{+}$ monocytes
- Dysfunctional HLA-DR^{lo}CD163^{+} and HLA-DR^{lo}S100A^{+} CD14^{+} monocytes in severe COVID-19
- Emergency myelopoiesis with immature and dysfunctional neutrophils in severe COVID-19

Schulte-Schrepping et al., 2020, Cell 182, 1419–1440
September 17, 2020 © 2020 Elsevier Inc.
https://doi.org/10.1016/j.cell.2020.08.001

CellPress

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COVID-19 VACCINE

Cell Stem Cell. 2010 November 5; 7(5): 618–630. doi:10.1016/j.stem.2010.08.012.

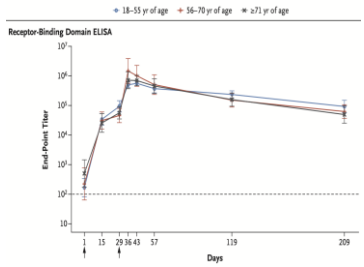
Highly efficient reprogramming to pluripotency and directed differentiation of human cells using synthetic modified mRNA

Luigi Warren[1,12], Philip D. Manos[2,3,12], Tim Ahfeldt[4,11], Yuin-Han Loh[2,5], Hu Li[6], Frank Lau[1,5], Wataru Ebina[1], Pankaj Mandal[1], Zachary D. Smith[7], Alexander Meissner[7], George Q. Daley[2,3,5,9], Andrew S. Brack[10], James J. Collins[8], Chad Cowan[4,6], Thorsten M. Schlaeger[2,3], and Derrick J. Rossi[1]

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19



The NEW ENGLAND JOURNAL of MEDICINE

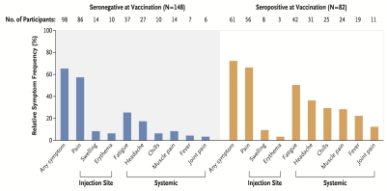
CORRESPONDENCE

SARS-CoV-2 Infection after Vaccination in Health Care Workers in California

Table 1. New SARS-CoV-2 Infections among Vaccinated Health Care Workers from December 16, 2020, through February 9, 2021.

Days after Vaccination	Vaccinated Persons		
	With New Infection (N = 379)	Tested (N = 14,604)*	Eligible for Testing (N = 36,659)†
	number		*number (percent)*
Dose 1			
Days 1–7	145	5794	35,673 (97.3)
Days 8–14	125	7844	34,404 (93.8)
Days 15–21	57	7958	32,667 (89.1)
Day 22 or later, before dose 2	15	4286	32,327 (88.2)
Dose 2			
Days 1–7	22	5546	23,100 (63.0)
Days 8–14	8	4909	16,082 (43.9)
Day 15 or later	7	4167	14,990 (40.9)

Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine



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SUBMITTING QUESTIONS

- **Many of you have submitted questions in advance. Thank you! If you have a question during the session, please follow the below instructions.**

- **Ask a question by web:**
  - Click "Ask a question"
  - Type your question
  - Click "Submit"

Due to time constraints, we may not be able to answer all questions. Thank you for understanding!

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LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:
To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online:
www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: infocenter@LLS.org
All email messages are answered within one business day.

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LLS EDUCATION & SUPPORT RESOURCES

Online Chats
Online Chats are free, live sessions, **moderated by oncology social workers**. To register for one of the chats below, or for more information, please visit **www.LLS.org/Chat**.

Education Videos
View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**.

Patient Podcast
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**.

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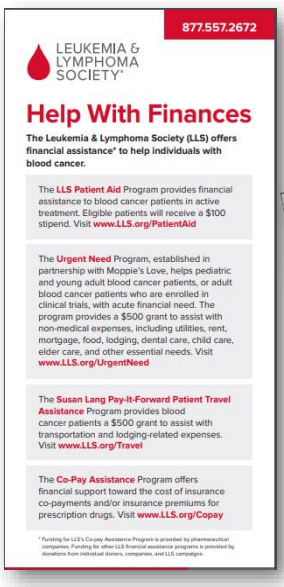
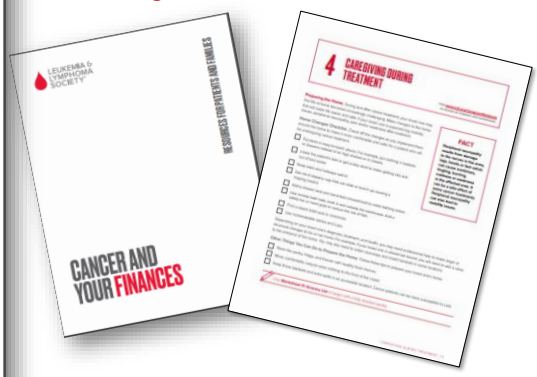


The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancer:
www.LLS.org/Finances



To order free materials: **www.LLS.org/Booklets**

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THANK YOU
We have one goal: A world without blood cancers
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