

Chances and Challenges of AI in a Hospital Setting

- There are strong needs for AI in a hospital to precision medicine, reduction of medical staff work load and increasing patient satisfaction level while there exist some obstacles to progress.
- From this viewpoint, some of the topics for discussion include but not limited:
 1. highly secure medical database and analytics technologies to extract useful medical information,
 2. AI-assisted automated medical record system and support for bilateral communication in informed consent,
 3. proof-of-concept study of AI hospital functions in clinical practice settings
 4. creation of new AI-tool platforms to assist the diagnosis, training, and communication of healthcare professionals.

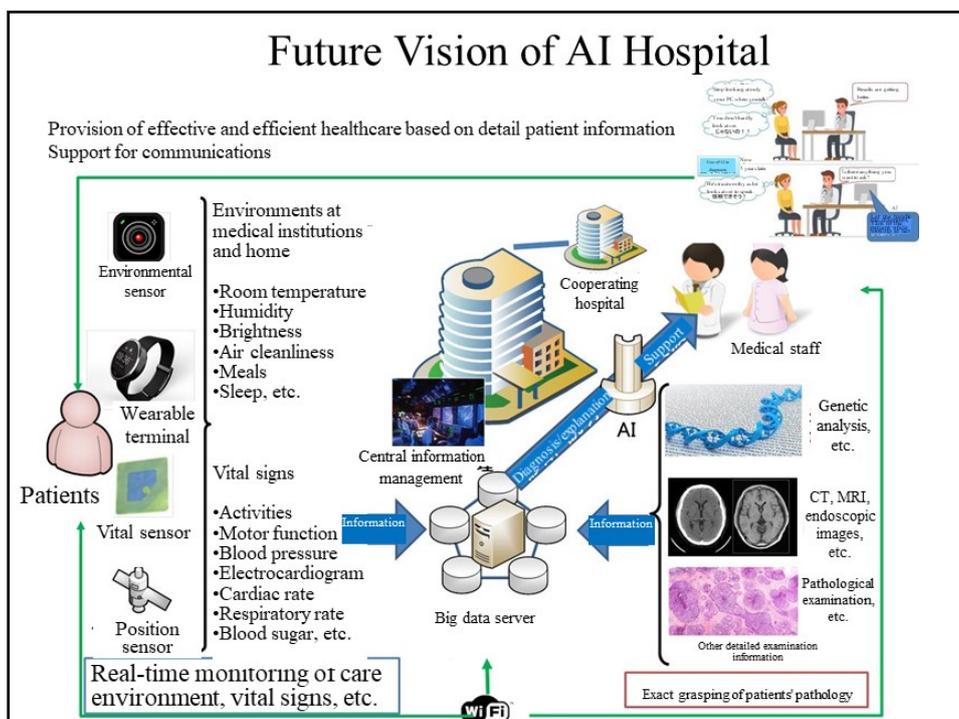
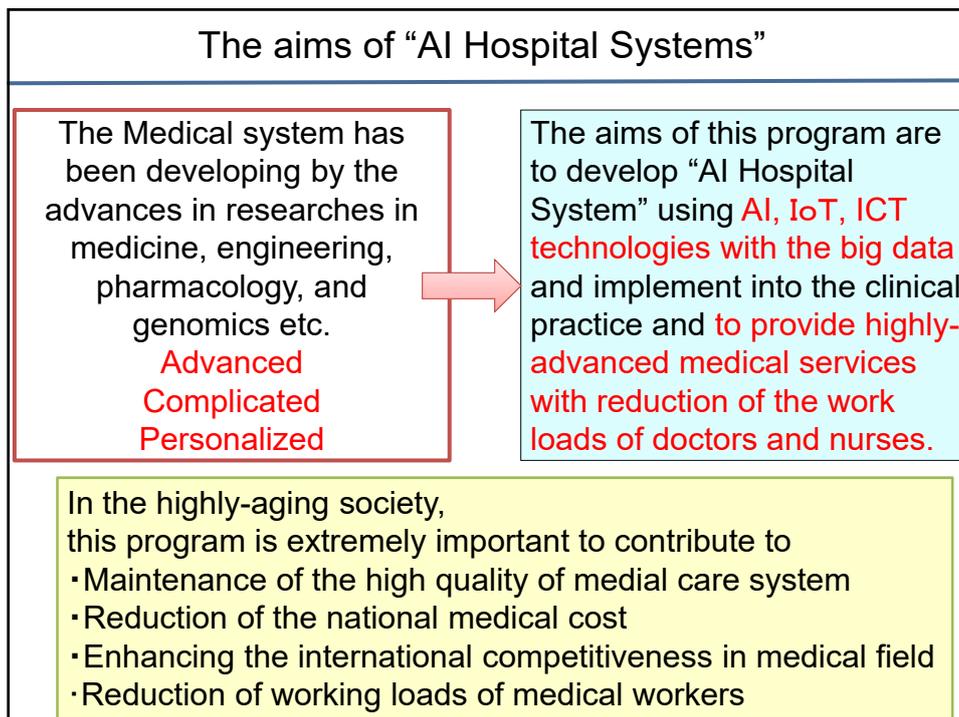
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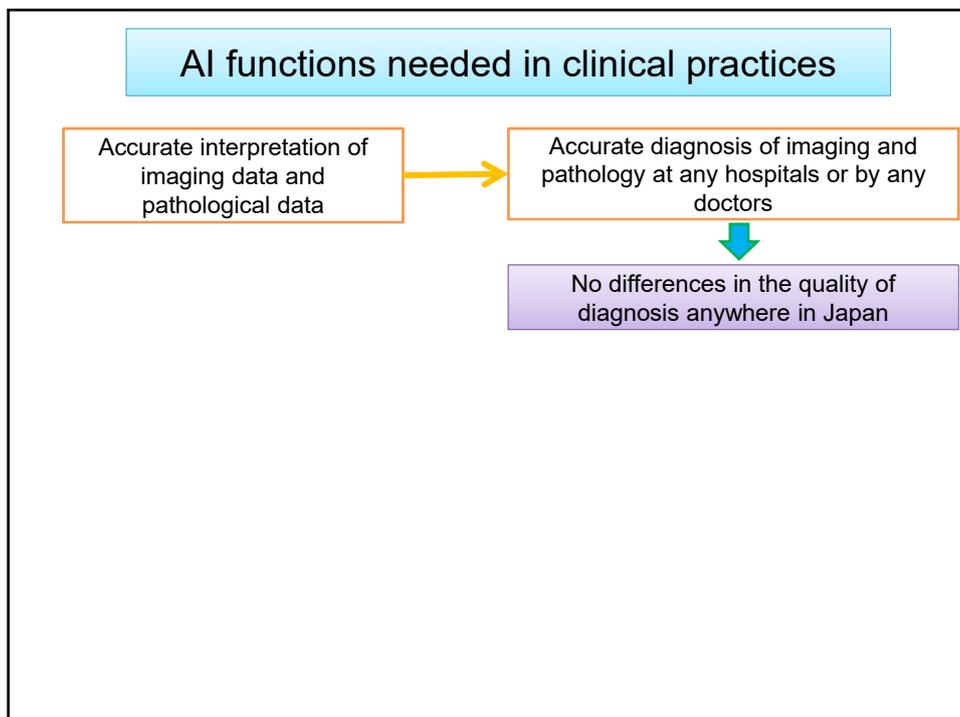
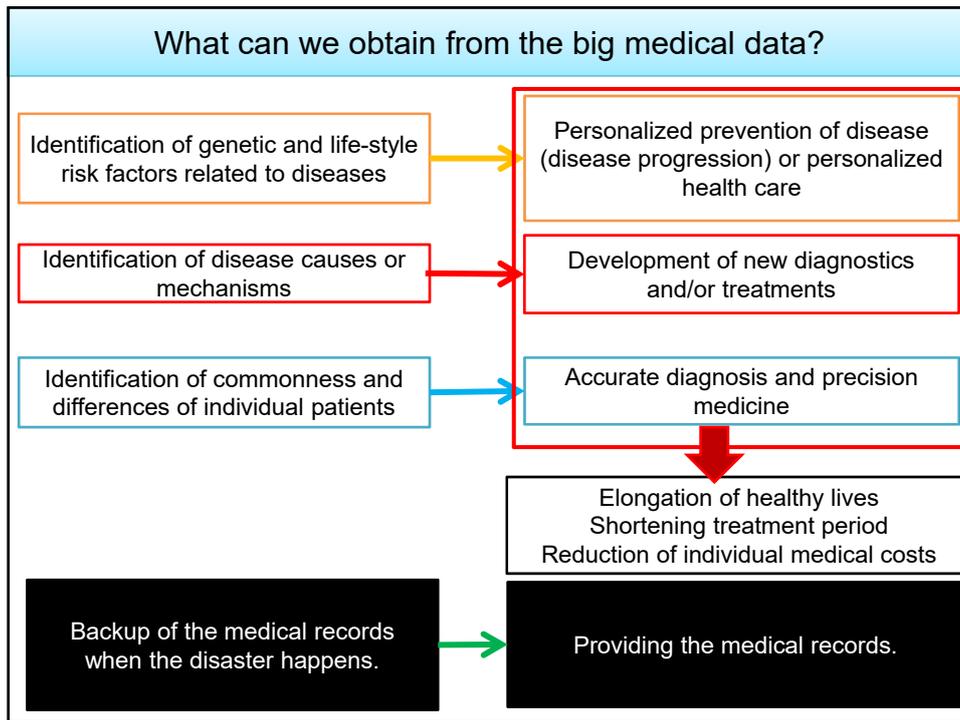
Strategic Innovation Promotion Program for "Development of AI Hospital System

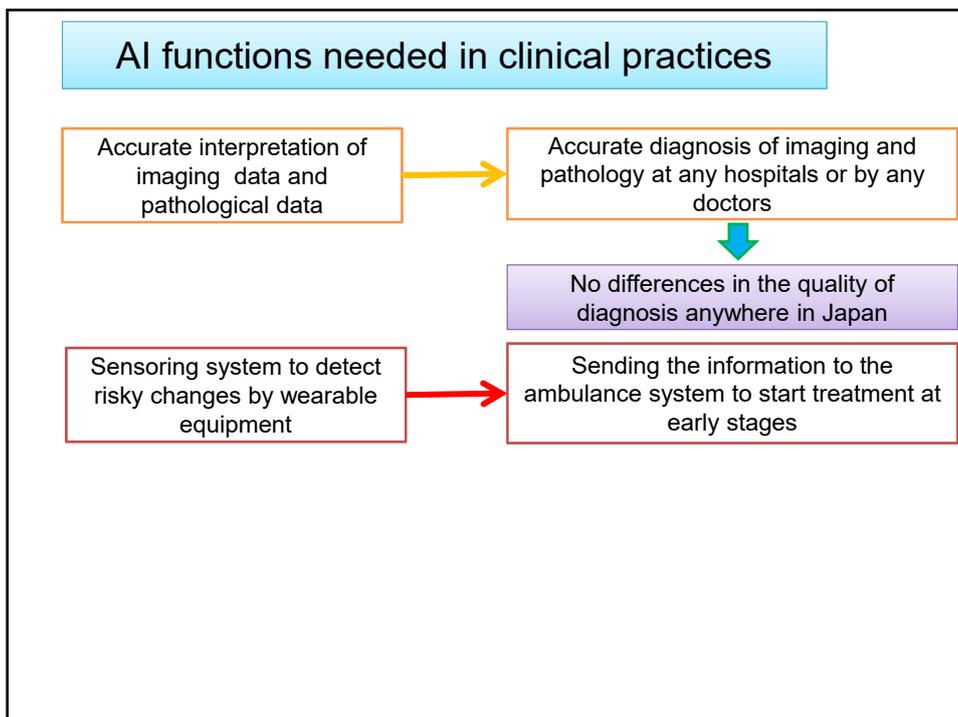
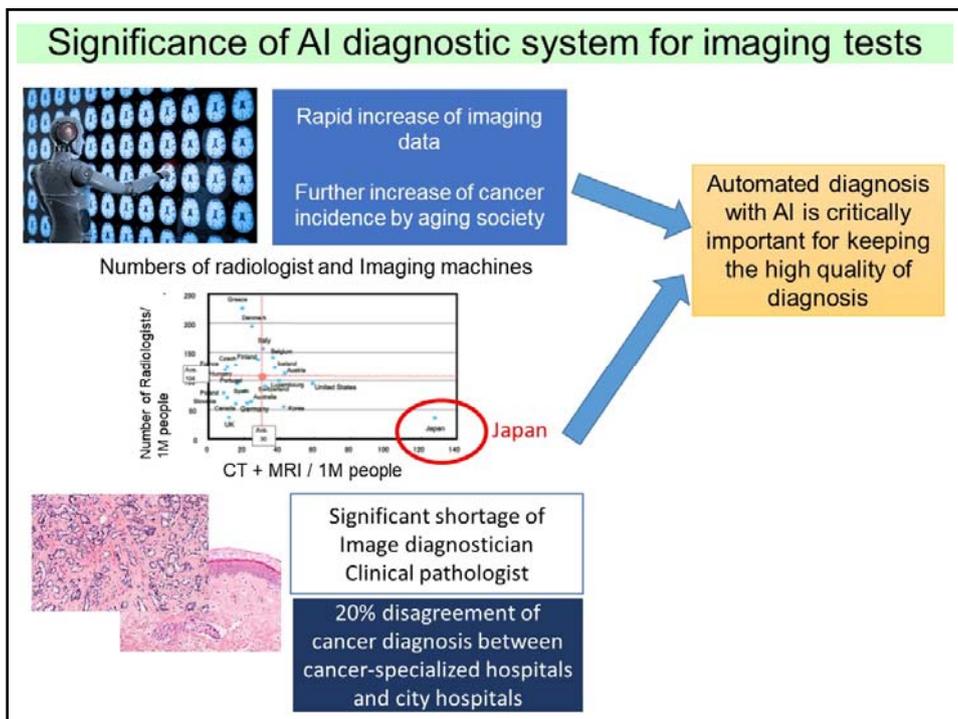
Satoru Miyano, PhD
(SubProgram Director)

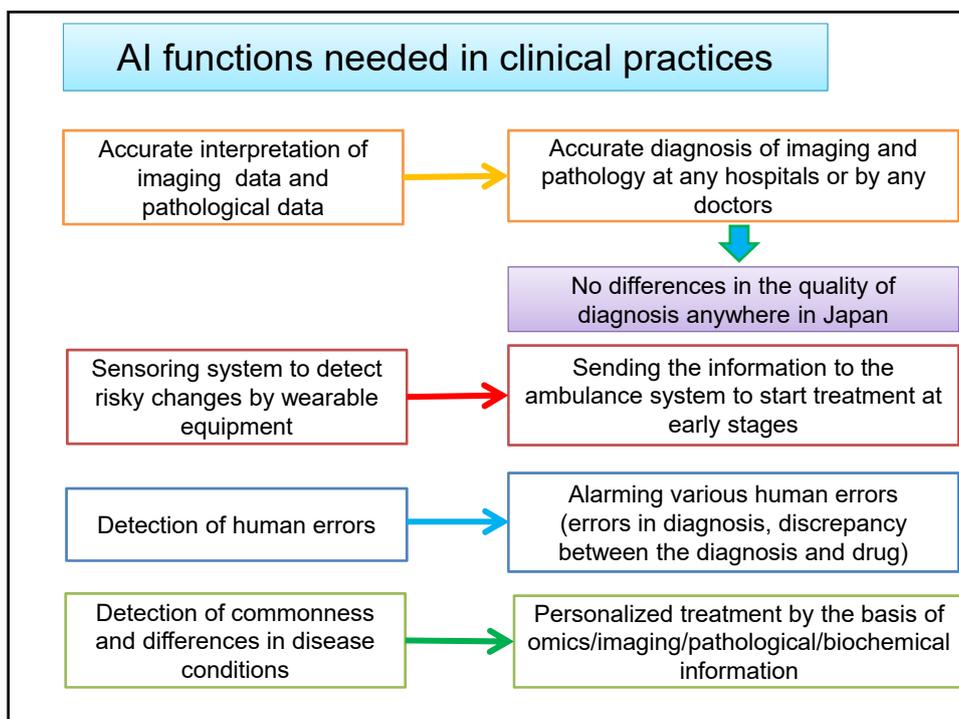
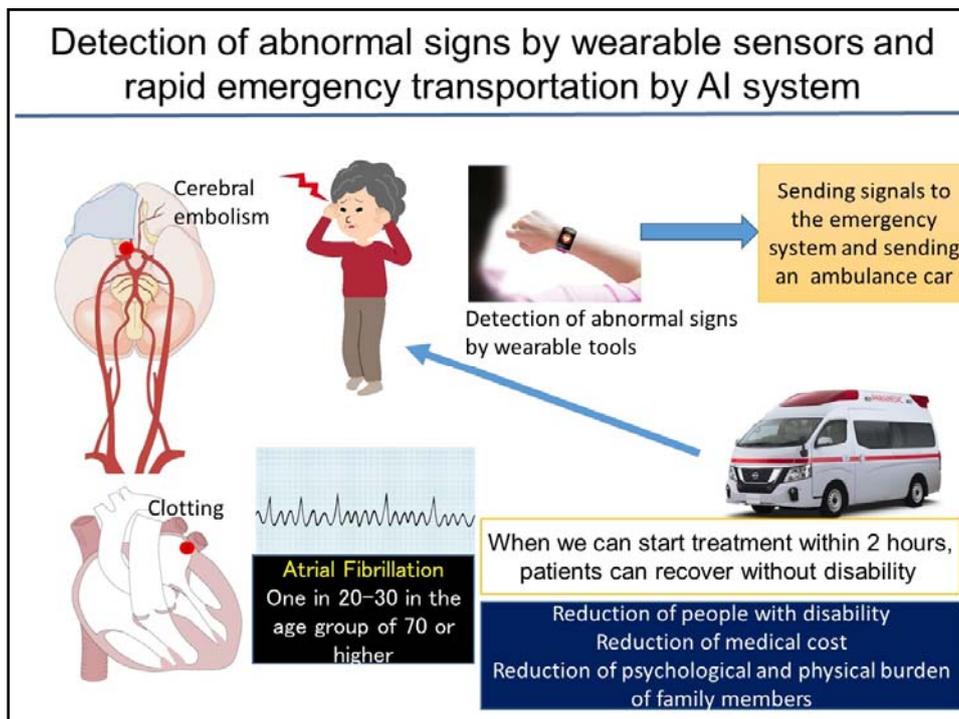
On behalf of Program Director
Yusuke Nakamura, MD, PhD

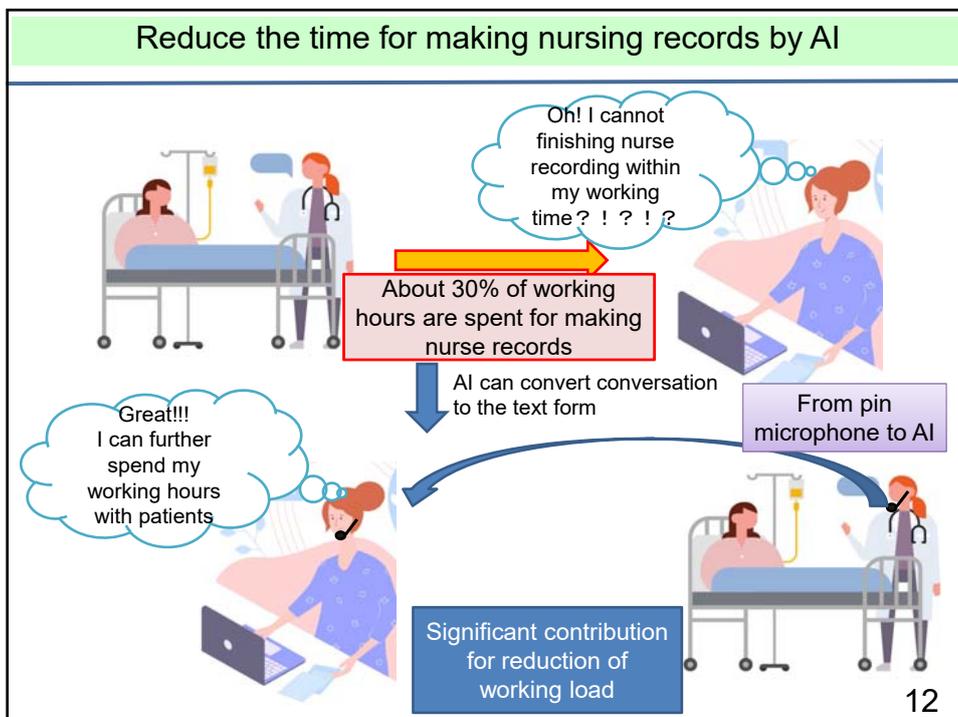
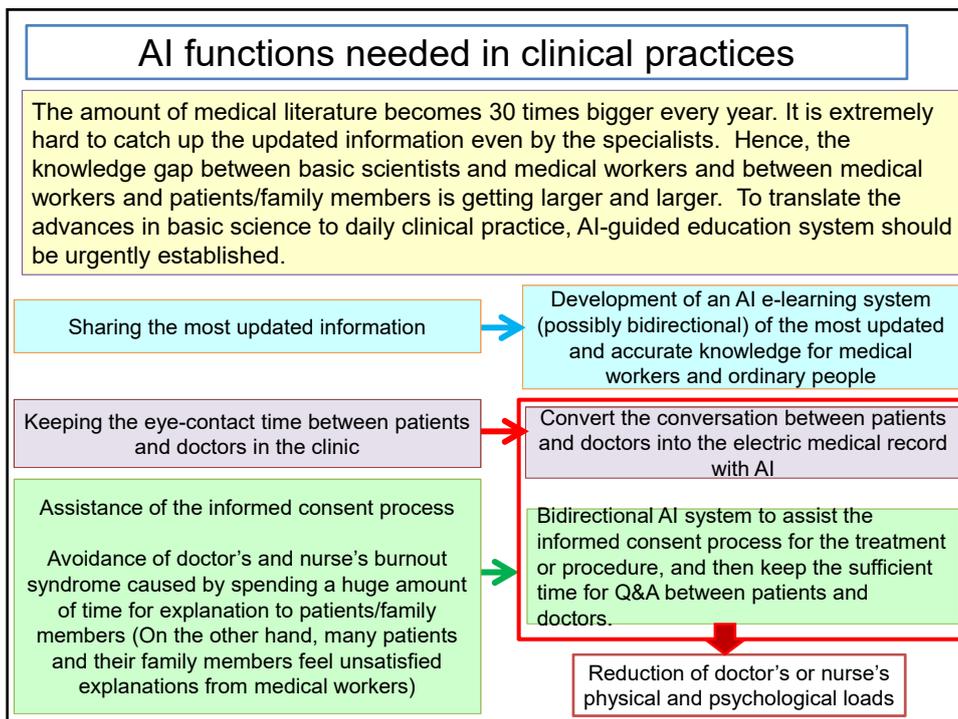
Budget	F2018 25M USD
	F2019 30M USD
	F2020 25M USD (expected)
	F2012 25M USD (expected)
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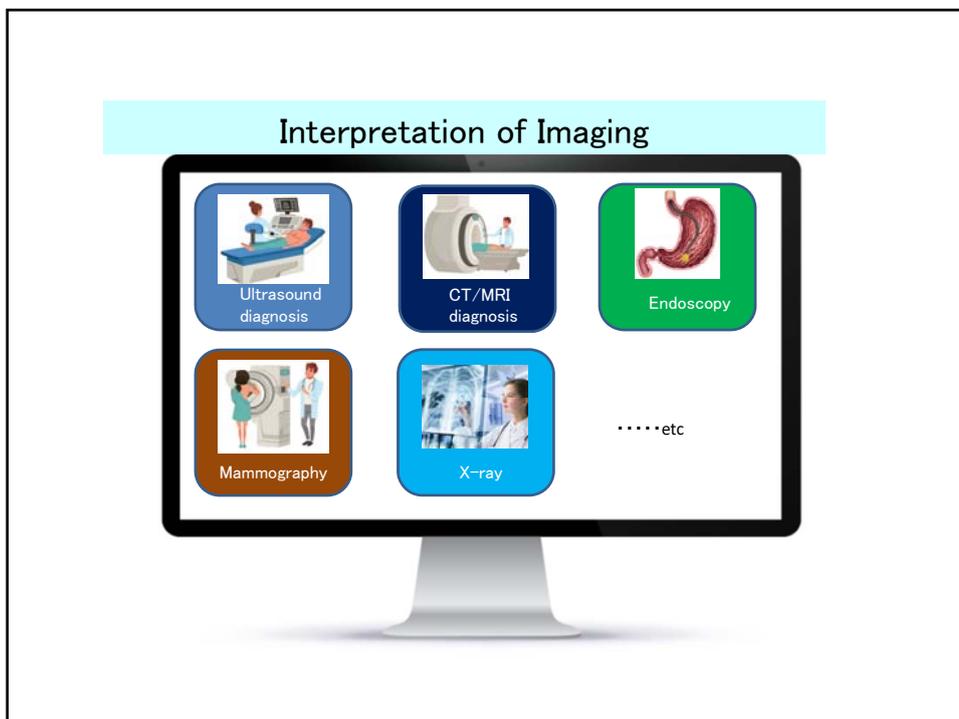
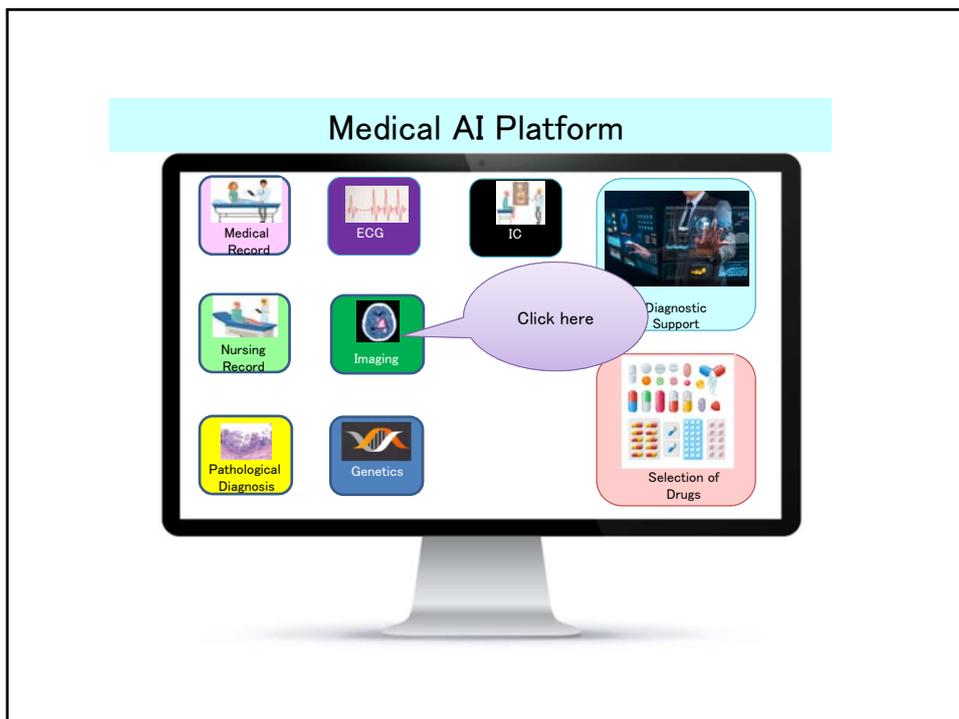


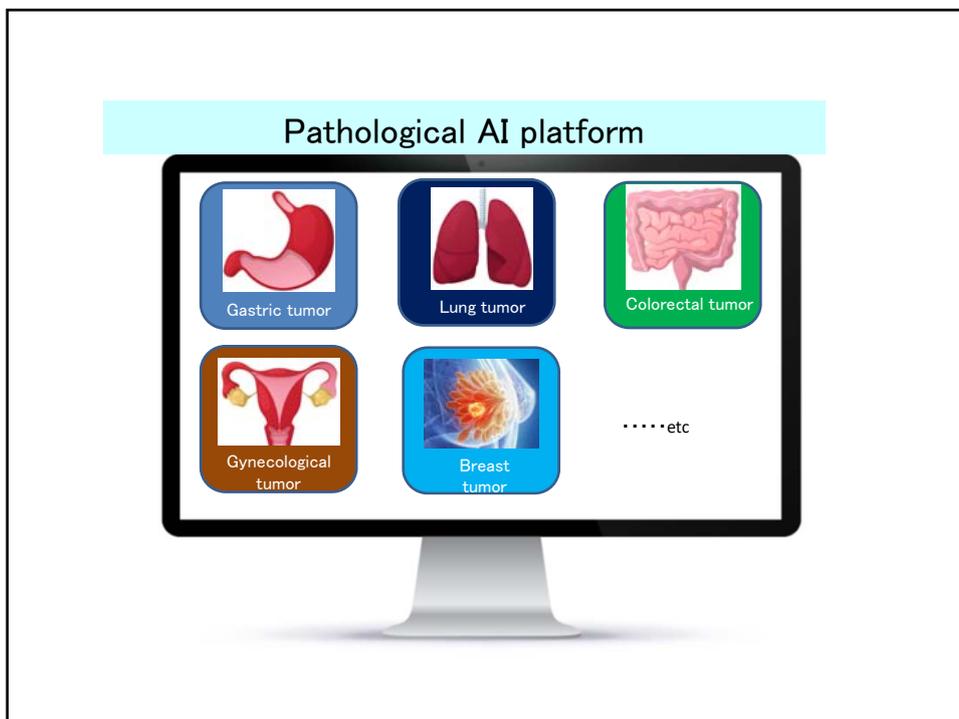
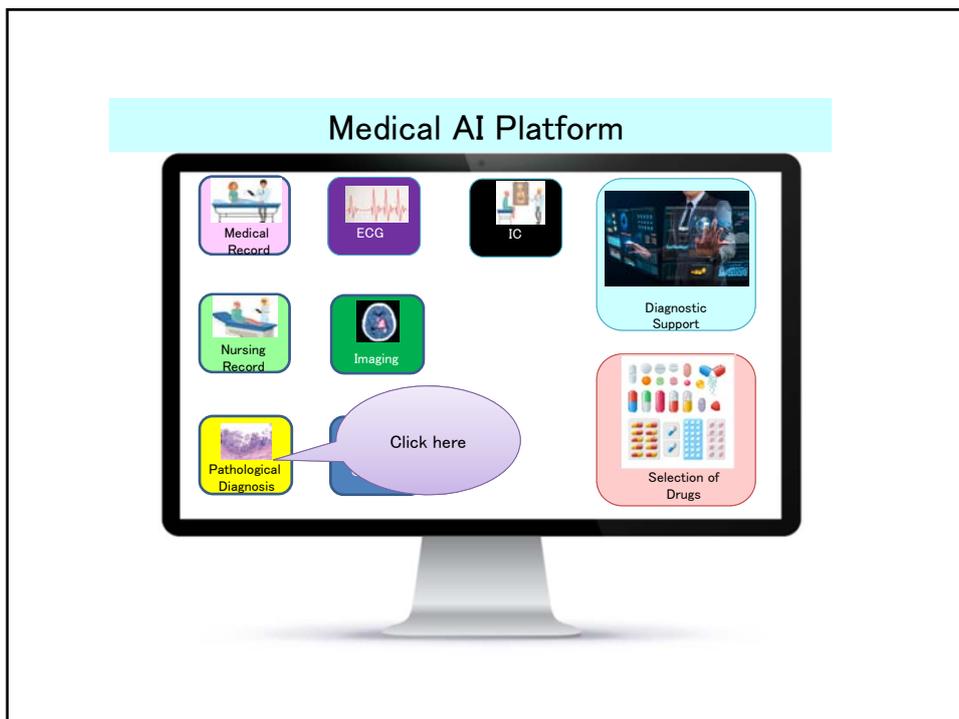








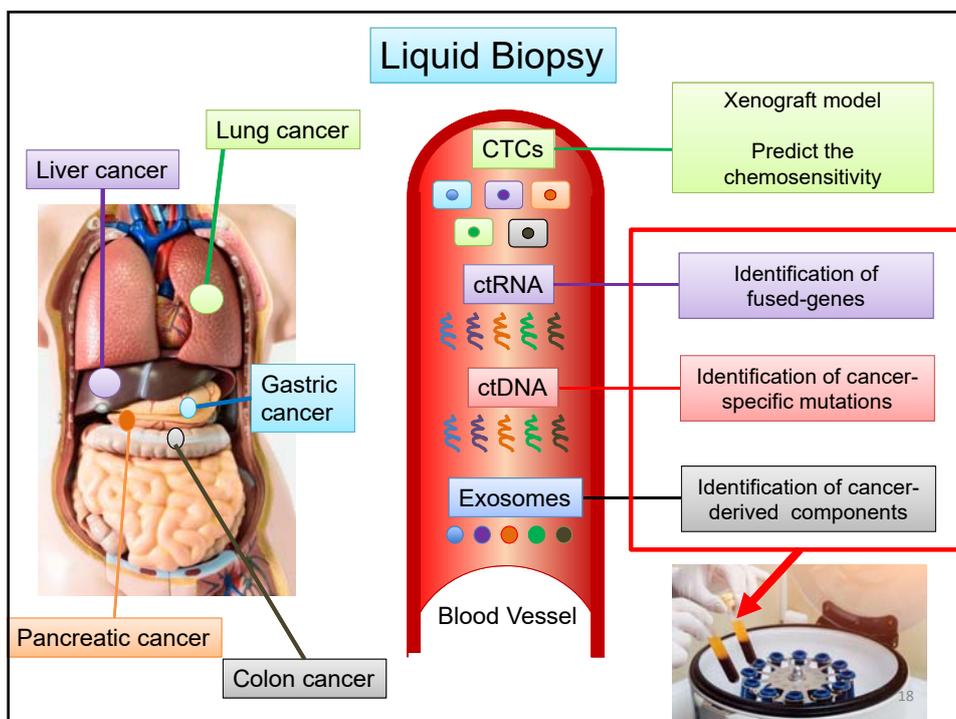


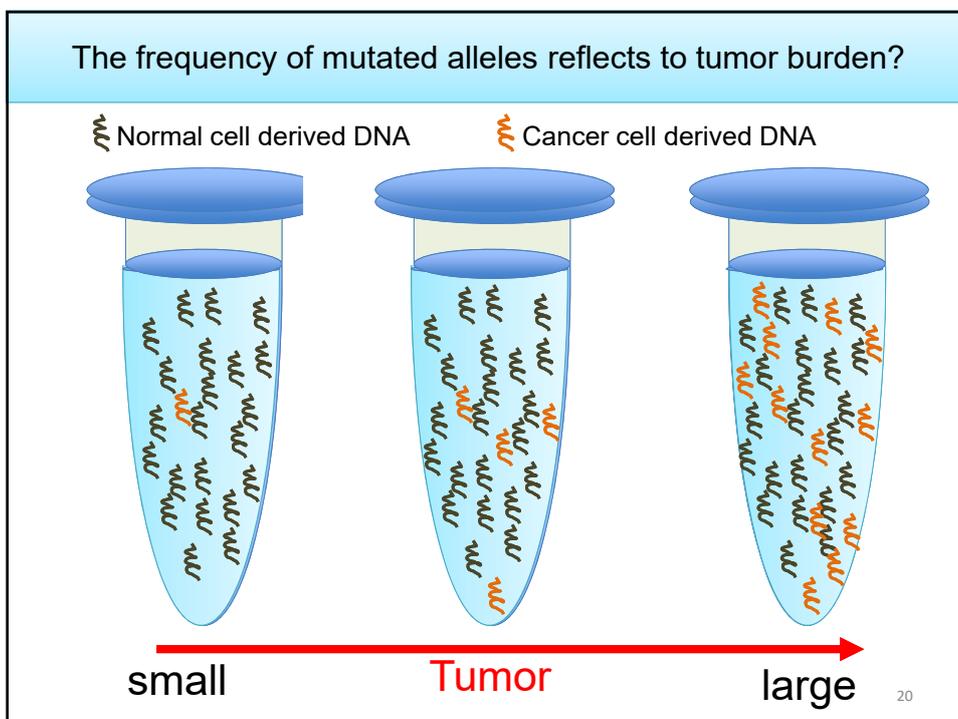
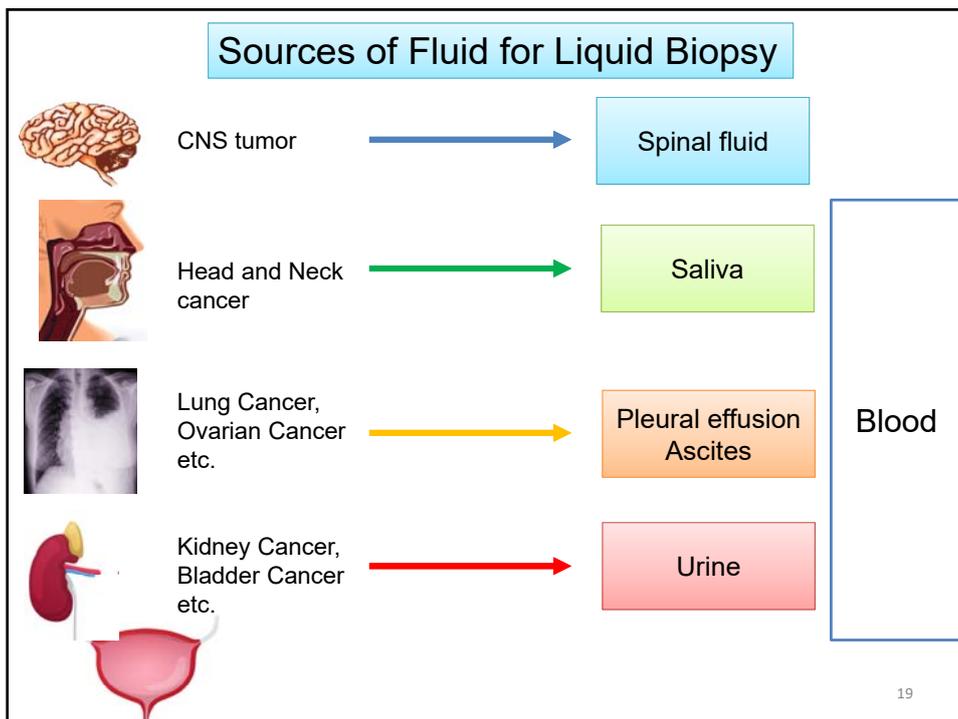


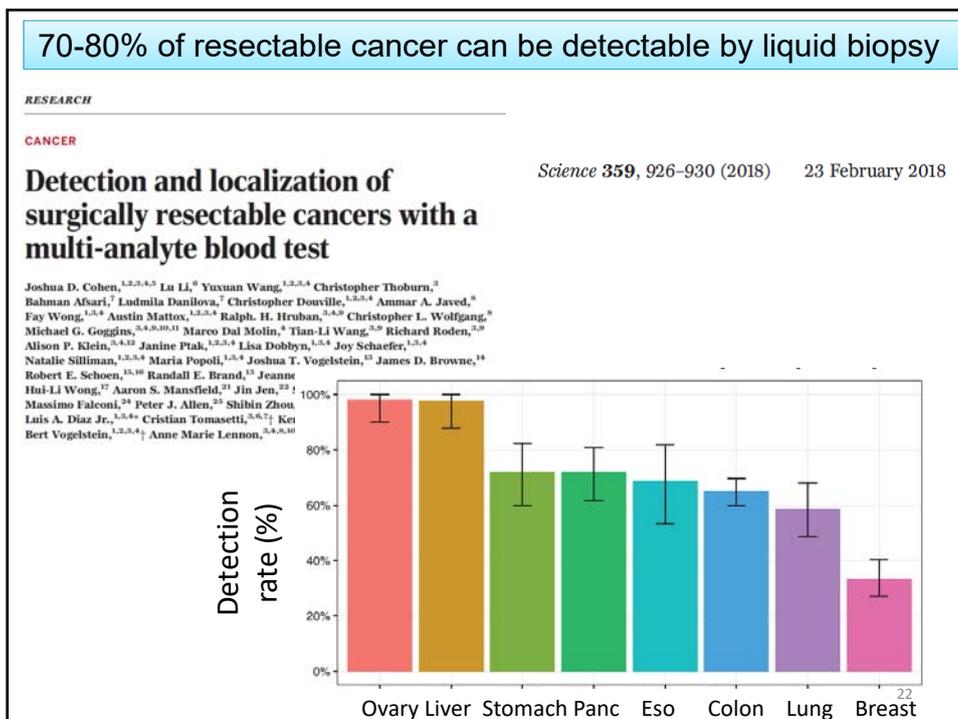
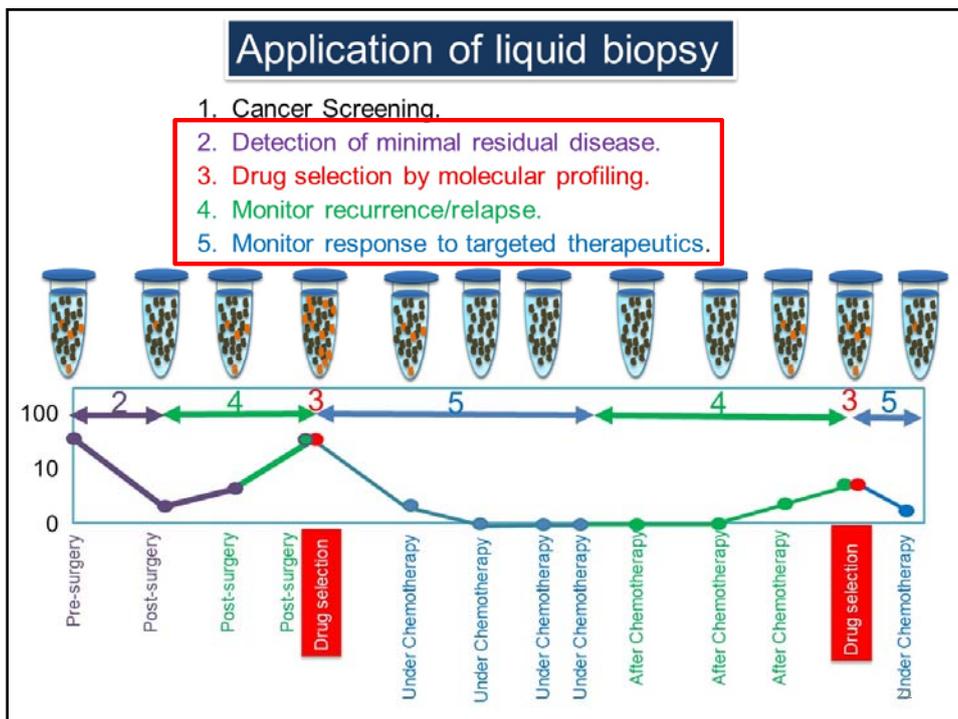
What we can do to improve cancer cure rate ?

1. Increase the cancer screening rate
(Cancer-risk-based personalized screening system)
(Development of an easier and cheaper screening method)
2. Earlier detection of relapse/recurrence, and earlier treatment
3. Selection of a right drug at a right time to a right patient
(an effective drug with minimum risk of adverse events)
(Ineffective drugs simply cause progression of cancer without any benefit to cancer patients)
4. Development of new classes of drugs
(Molecular-targeted drugs)
(Immunotherapy; Neoantigen vaccine • CAR-T therapy • TCR-engineered T cell therapy)

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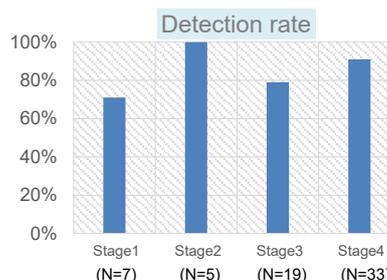




Liquid biopsy of 67 lung cancer samples

- Mutations of at least one gene were detected in **58/67 (87%)** of lung cancer cases.

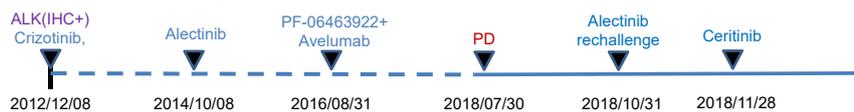
Gene	%_patients	Gene	%_patients
<i>TP53</i>	63%	<i>CDK6</i>	4%
<i>EGFR</i>	24%	<i>CCND2</i>	4%
<i>KRAS</i>	10%	<i>GNAS</i>	4%
<i>FGFR3</i>	10%	<i>CCND3</i>	3%
<i>MET</i>	7%	<i>BRAF</i>	3%
<i>PIK3CA</i>	6%	<i>CDK4</i>	3%
<i>IDH2</i>	6%	<i>ERBB2</i>	3%
<i>APC</i>	4%	<i>FBXW7</i>	3%
<i>FGFR1</i>	4%	<i>Others</i>	12%



Low et al. ²³

Clinical importance of mutation detection

JFCR-LU-06; monitoring JFCR-LU-17

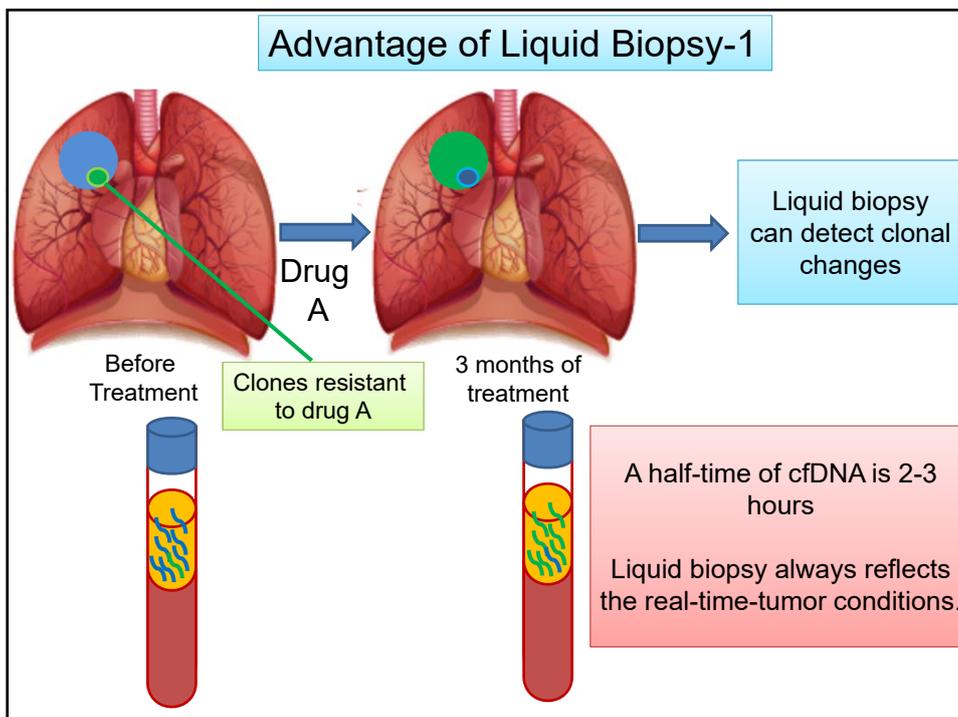
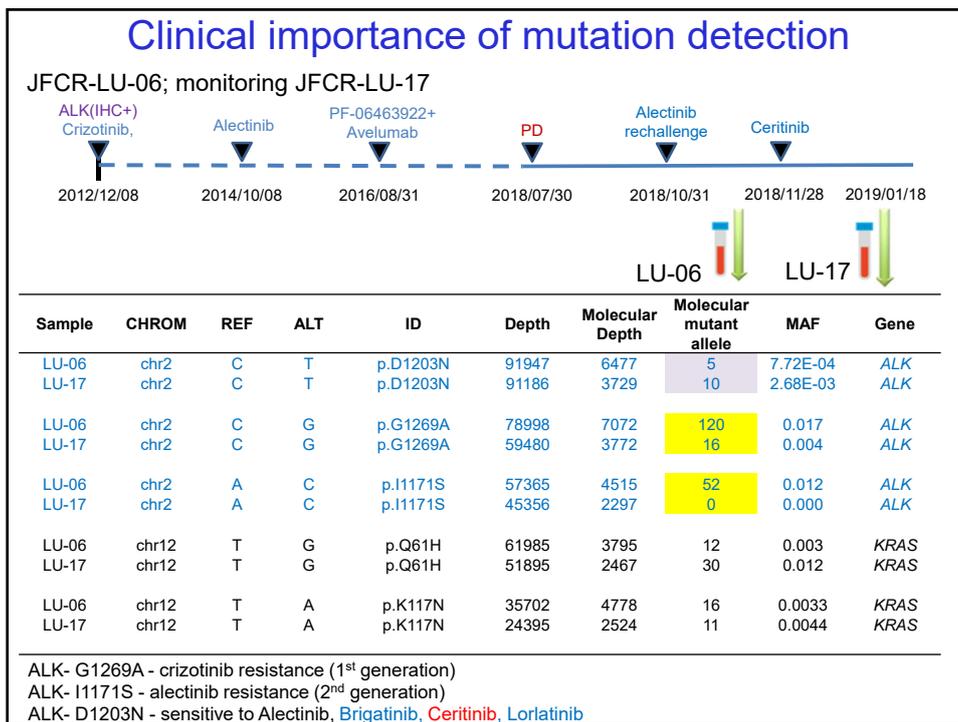


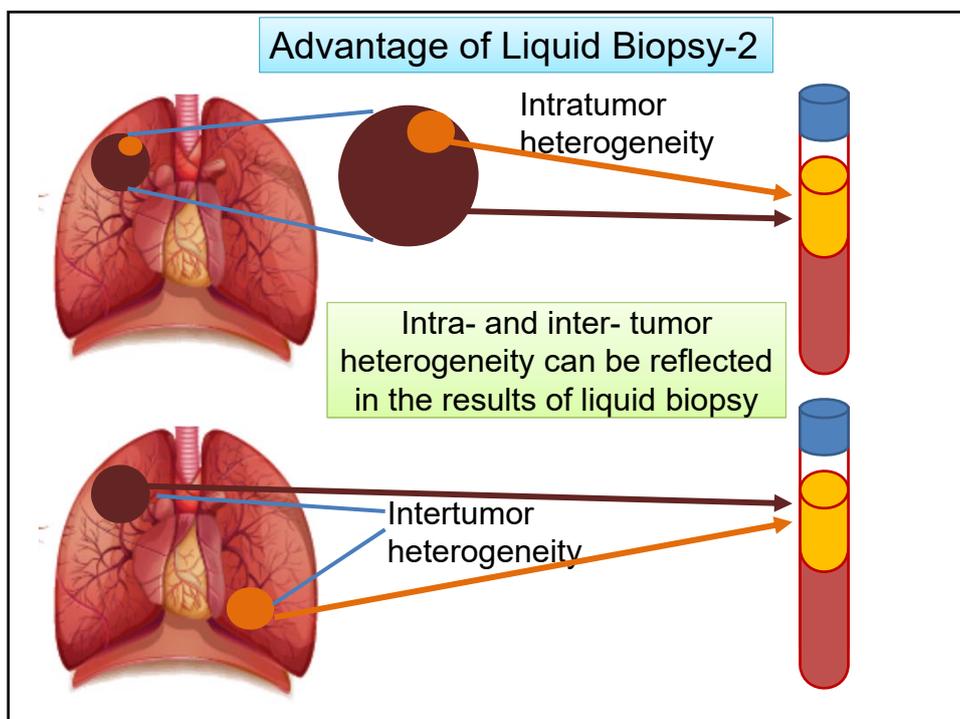
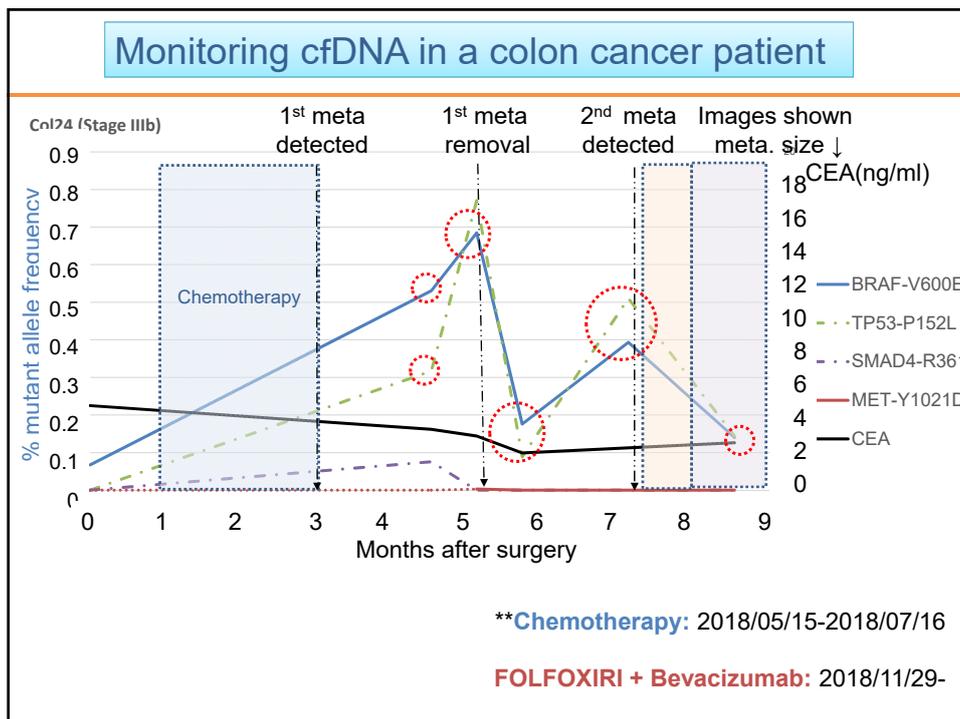
Sample	CHROM	REF	ALT	ID	Depth	Molecular Depth	Molecular mutant allele	MAF	Gene
LU-06	chr2	C	T	p.D1203N	91947	6477	5	7.72E-04	ALK
LU-06	chr2	C	G	p.G1269A	78998	7072	120	0.017	ALK
LU-06	chr2	A	C	p.I1171S	57365	4515	52	0.012	ALK
LU-06	chr12	T	G	p.Q61H	61985	3795	12	0.003	KRAS
LU-06	chr12	T	A	p.K117N	35702	4778	16	0.0033	KRAS

ALK- G1269A - crizotinib resistance (1st generation)

ALK- I1171S - alectinib resistance (2nd generation)

ALK- D1203N - sensitive to Alectinib, Brigatinib, Ceritinib, Lorlatinib





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Objective response rates by treatment with antibodies targeting the PD-1/PD-L1 pathway

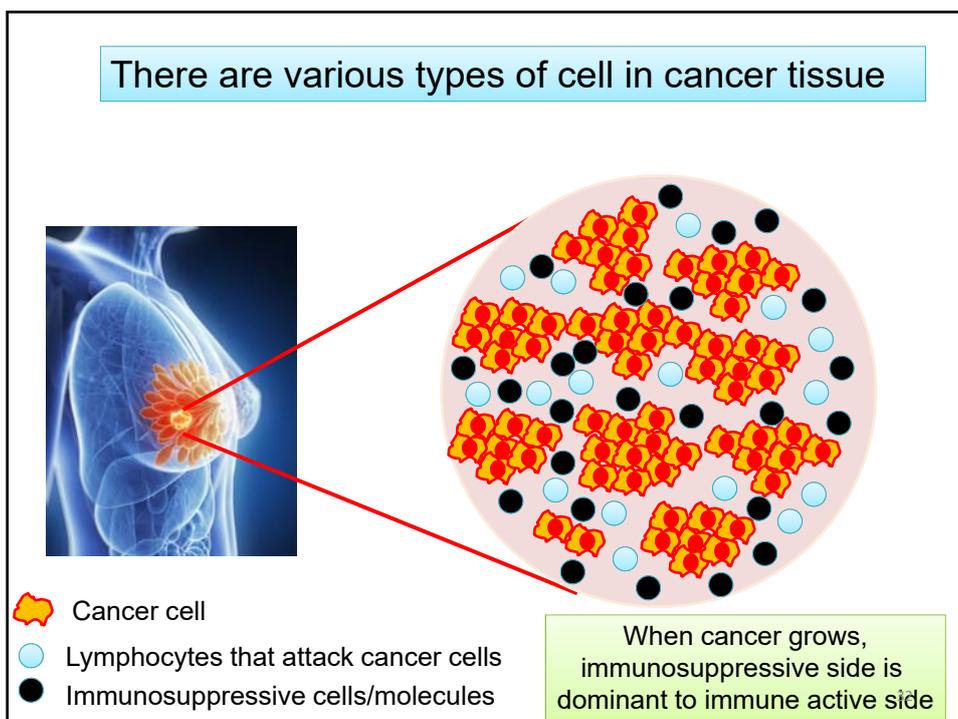
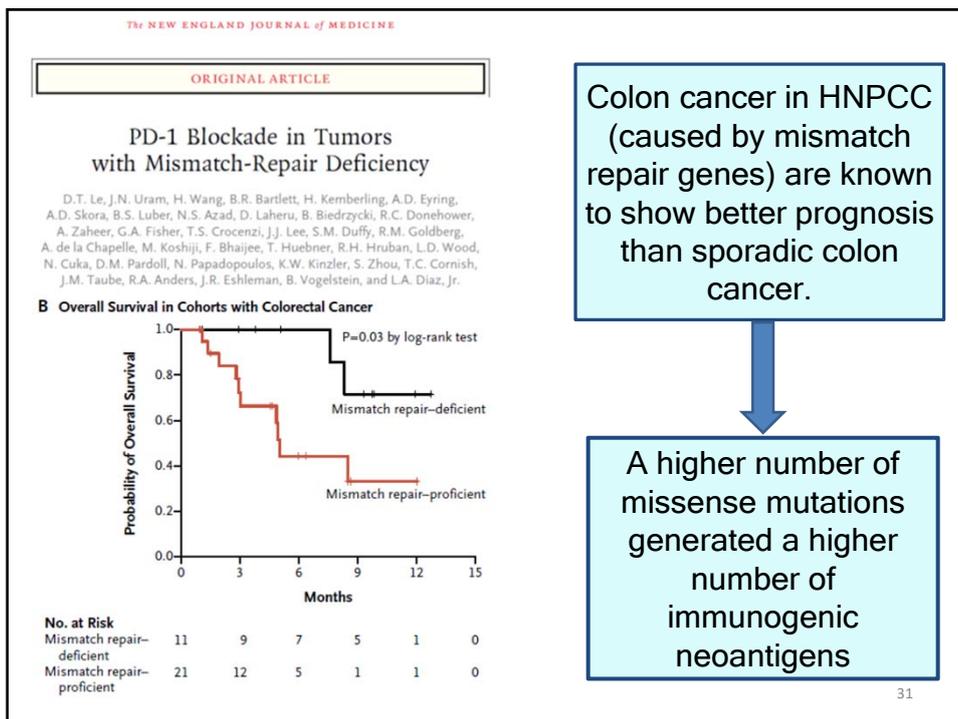
Type of Cancer	ORR (%)
Melanoma	20-32%
Stomach	31%
Esophagus	30%
Bladder	25-26%
Kidney	25%
SCLC	18-25%
Head & Neck	12-25%
NSCLC	14-19%
Breast	12-19%
Ovary	10-15%
Uterus (endometrial)	13%
Uterus (cervix)	13%
Liver	9%

Although treatment targeting immunecheckpoint molecules reveals durable effect, the majority of patients can not have any benefit from these therapies, which are very expensive.

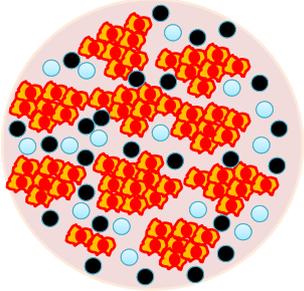


- (1) We need to select patients who can expect to have benefit.
- (2) We need to develop the way to further enhance the effect of these treatments or another types of immunotherapy to eradicate cancer cells.

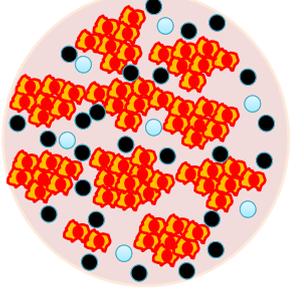
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There are various types of cell in cancer tissue



When cancer grows, immunosuppressive side is dominant to immune active side.



In some cancers, there is very weak anti-cancer immune reactive cells.

- Cancer cell
- Lymphocytes that attack cancer cells
- Immunosuppressive cells/molecules

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79 year old with 60 pack year smoking history who presented with chronic cough in April 2015

4/21/2015

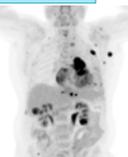


4/30/2015



Squamous cell carcinoma

5/12/2015

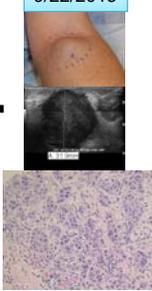


Widespread metastases in Chest Abdomen

C1 = 9/25/2015
C2 = 10/9/2015



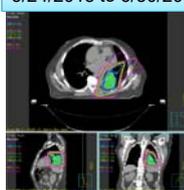
9/22/2015



8/28/2015



6/24/2015 to 6/30/2015

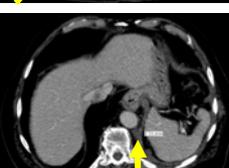


Chest XRT - total of 42 Gy

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Marked tumor shrinkage after 5 doses of anti-PD-1 antibody

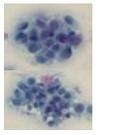
	8/28/2015	11/30/2015 after C5	
right adrenal metastasis of 4.6 cm			no longer measurable
Right peri-renal lesion of 4.6 cm			Right peri-renal lesion has decreased to 3.5 cm
Left lower quadrant mass of 1.9 cm			necrotic mass of 1.3 cm

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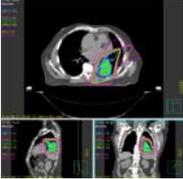
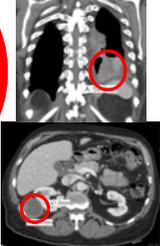
79 year old with 60 pack year smoking history who presented with chronic cough in April 2015

4/21/2015 → 4/30/2015 → 5/12/2015

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Widespread metastases in Chest Abdomen

6/24/2015 to 6/30/2015 → 8/28/2015 → 9/22/2015

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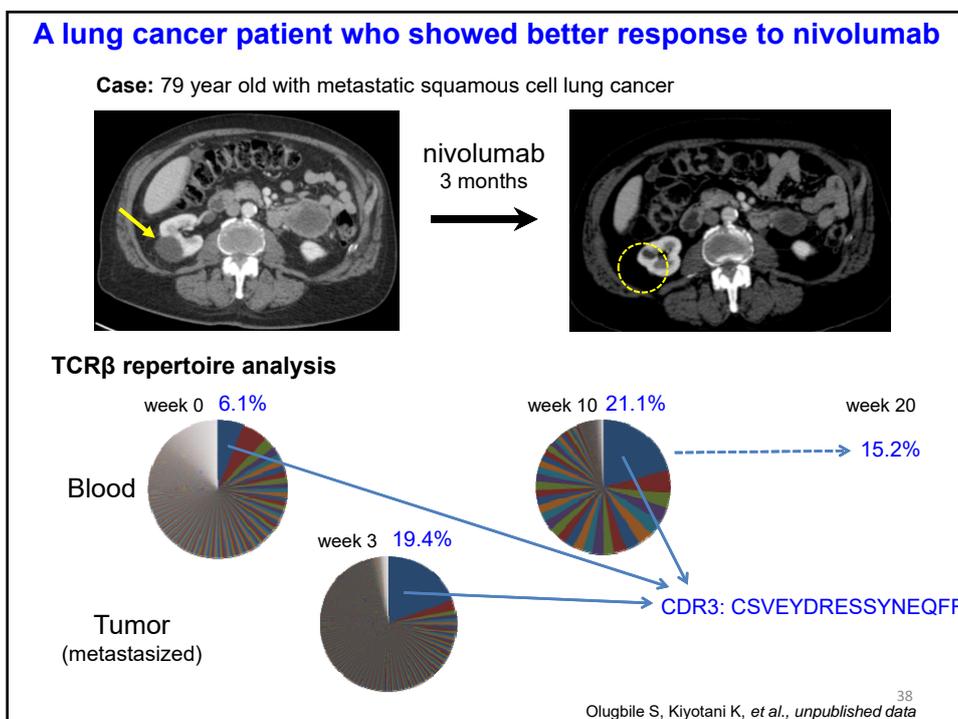
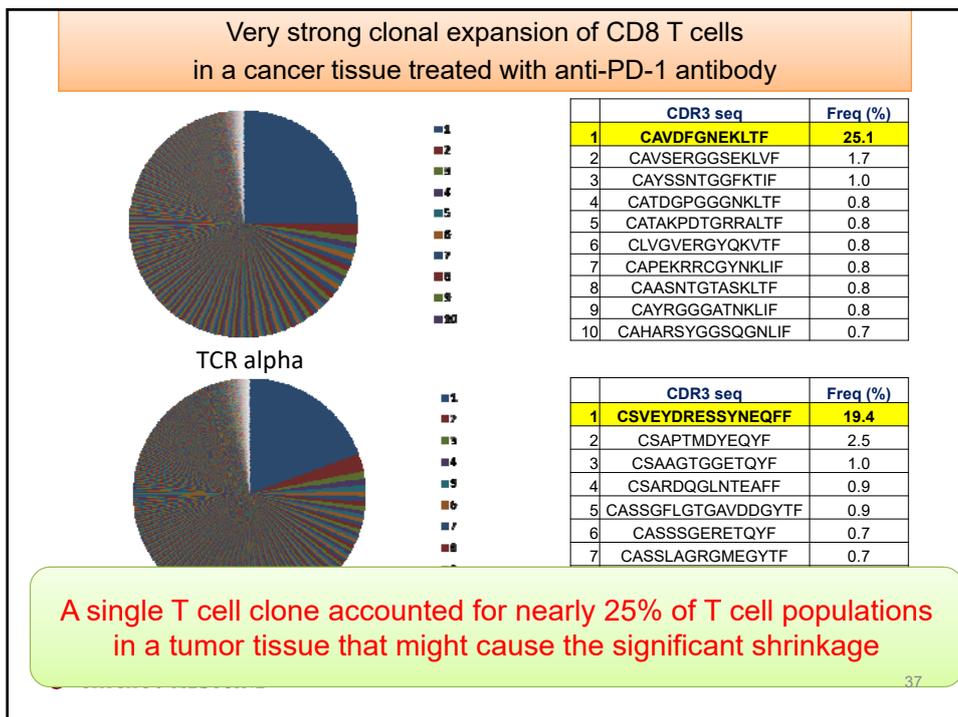
Chest XRT - total of 42 Gy

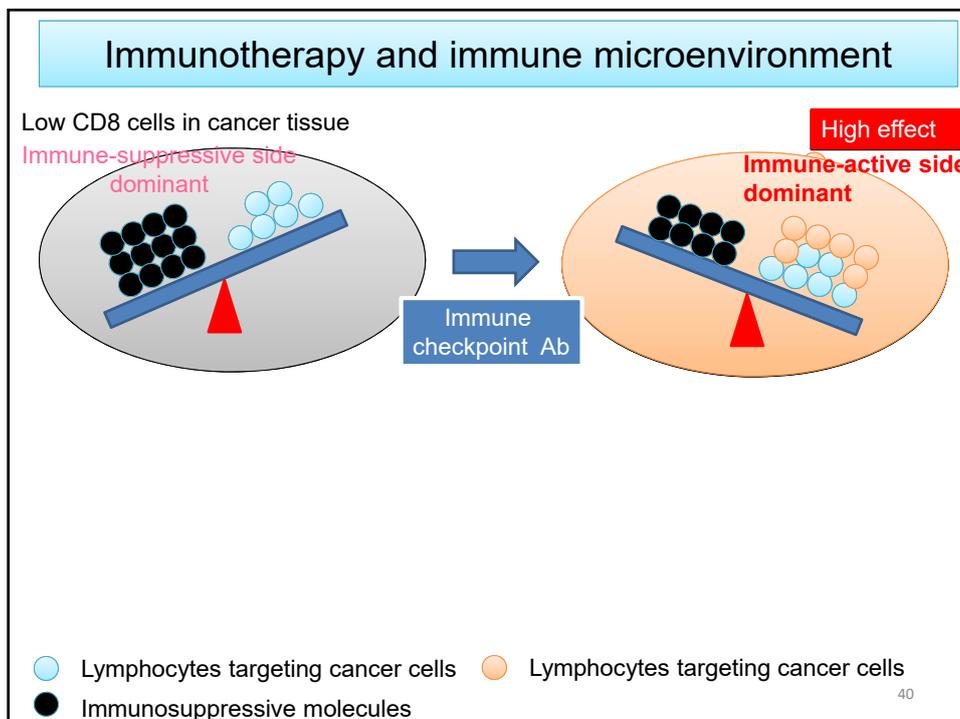
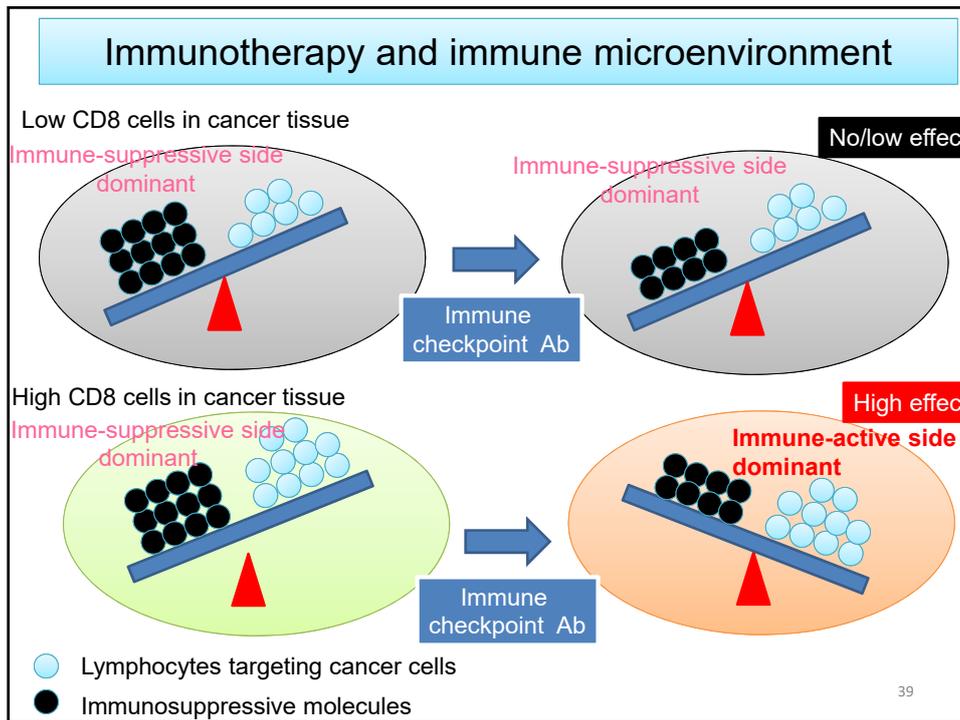
C1 = 9/25/2015
C2 = 10/9/2015



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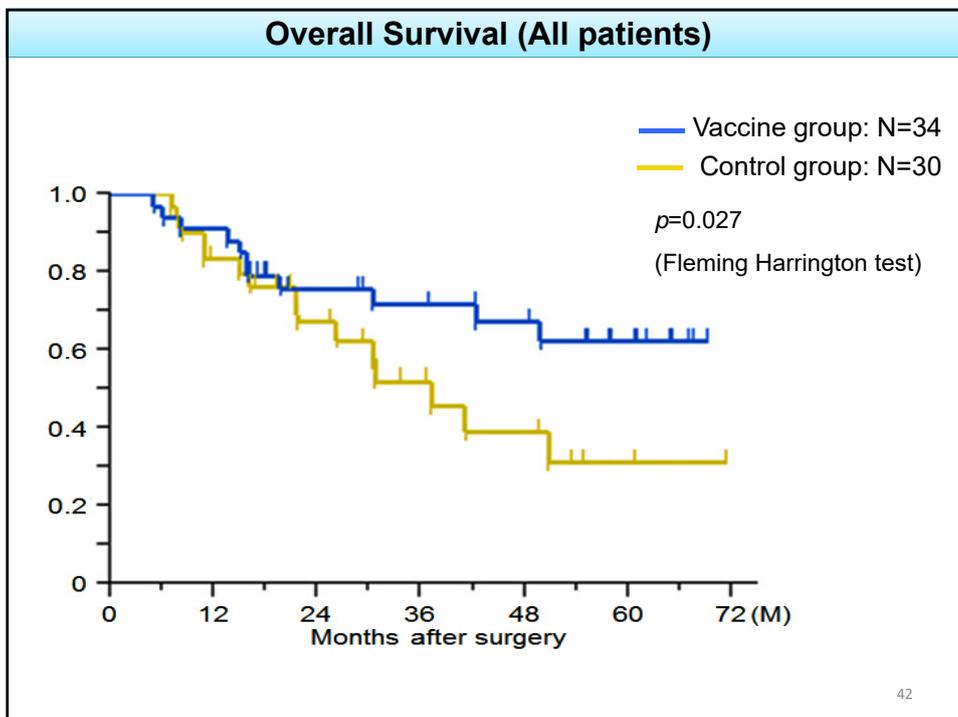




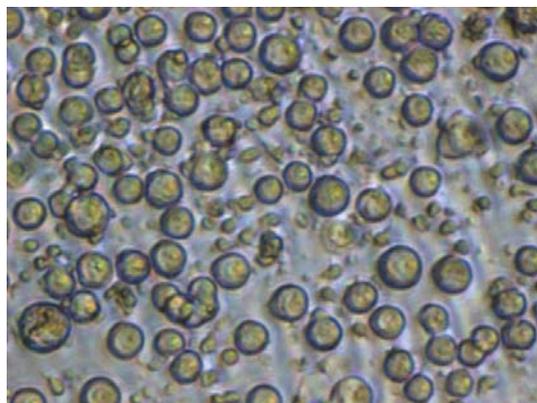
Two possible cancer vaccines to activate lymphocytes targeting cancer cells

	Neoantigens (Mutation-specific)	Oncoantigens (Shared antigens)
Specificity (Safety)	Highly specific to cancer cells	Specific? (some normal cells?)
Prevalence	Personalized (Private except some like KRAS)	Shared (HLA-restricted)
Immunogenicity	High ? (less evidences)	High (more evidences)

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Killing of TE1 esophageal cancer cells by URLC10-specific CTLs derived from a patient treated with cancer vaccine



Large cells: Esophageal Cancer Cells TE1
Small cells: peptide-specific CTLs

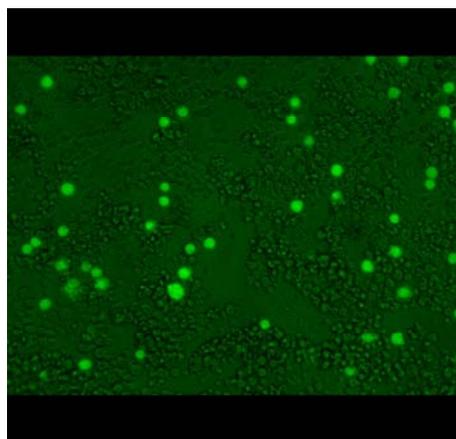
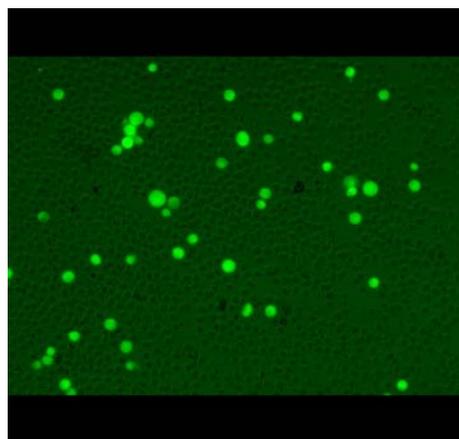
By Drs. Hiroki Yamaue and Makoto Iwahashi
At Wakayama Medical University

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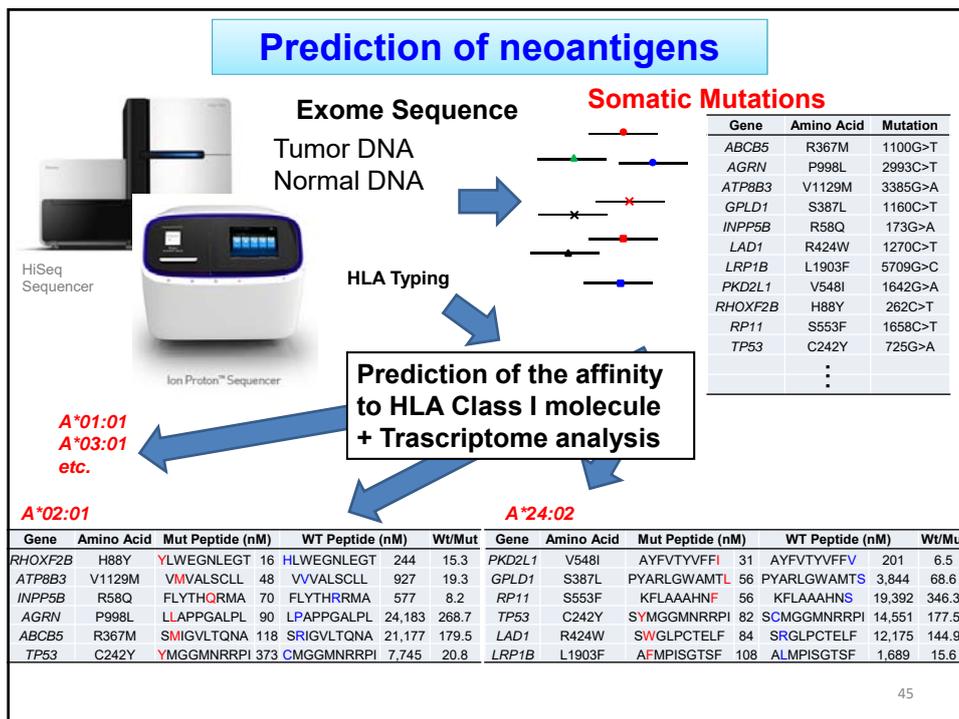
Cytotoxic Activity of UBE2T-specific T cells

BT549 : HLA-A*24:02 Negative

SW480 : HLA-A*24:02 Positive



UBE2T specific T cells killed HLA-A*24 SW480 cells after strong chemotaxis, but not HLA-A unmatched BT549 cells:⁴



LETTER

https://doi.org/10.1038/s41586-018-0792-2 2019.01.10

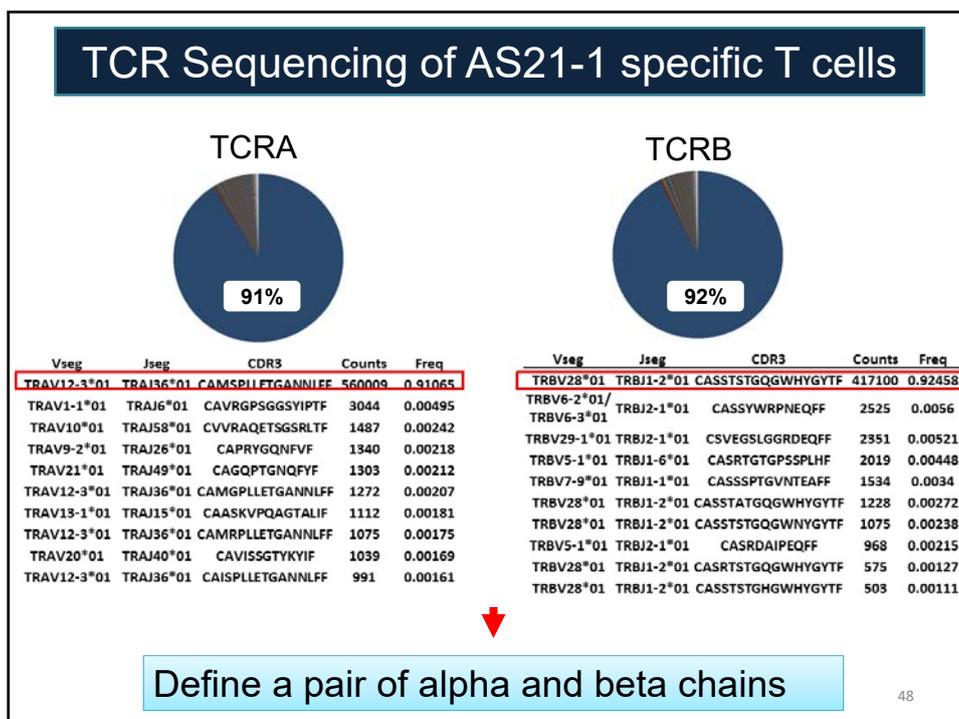
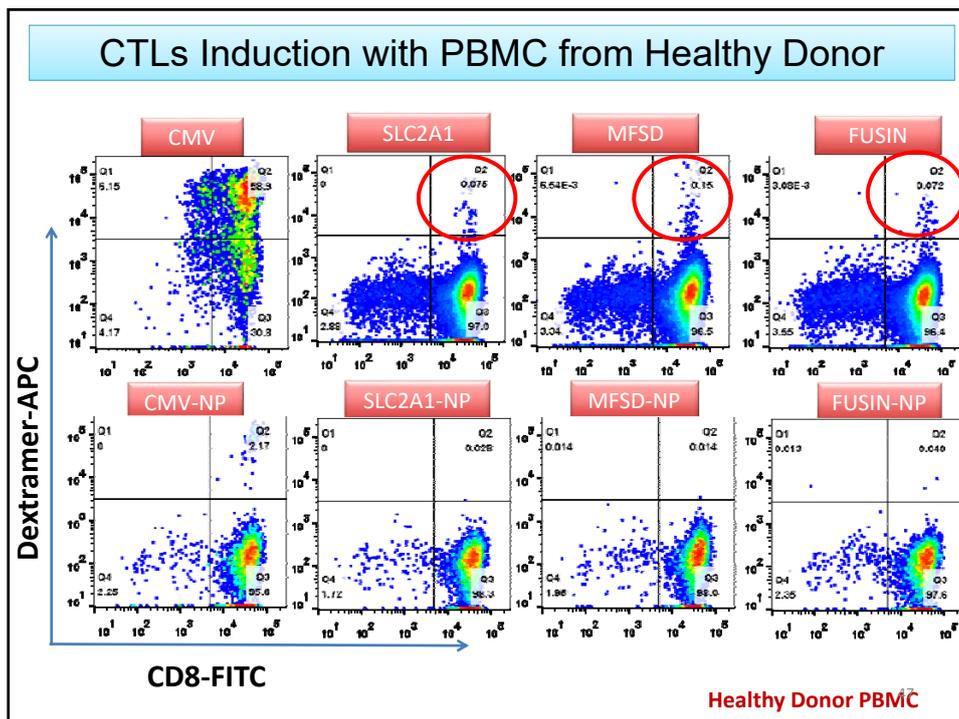
Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial

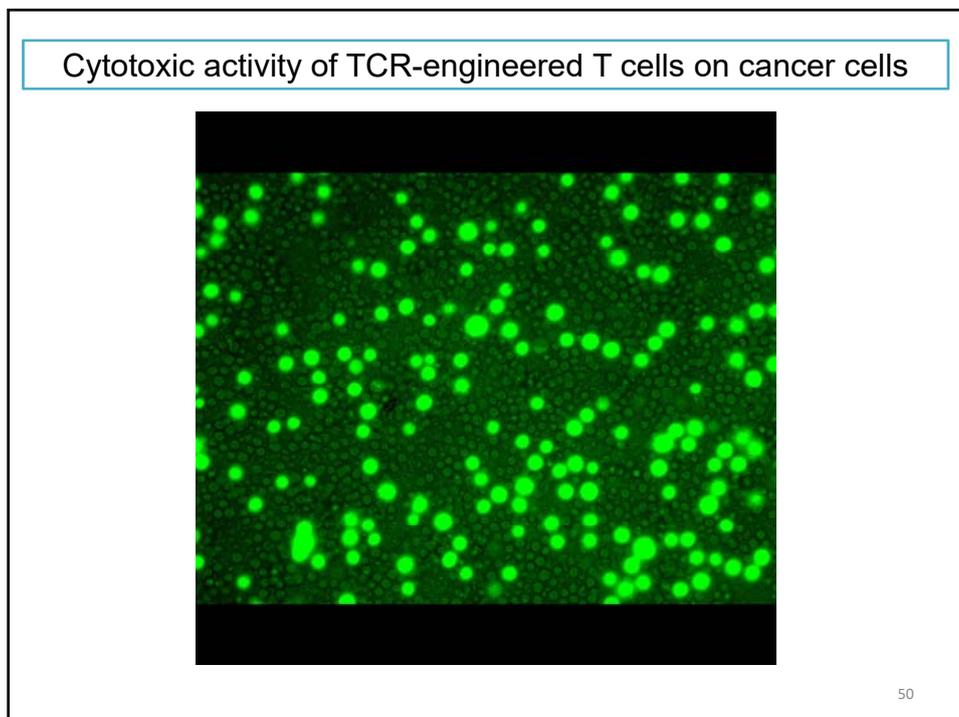
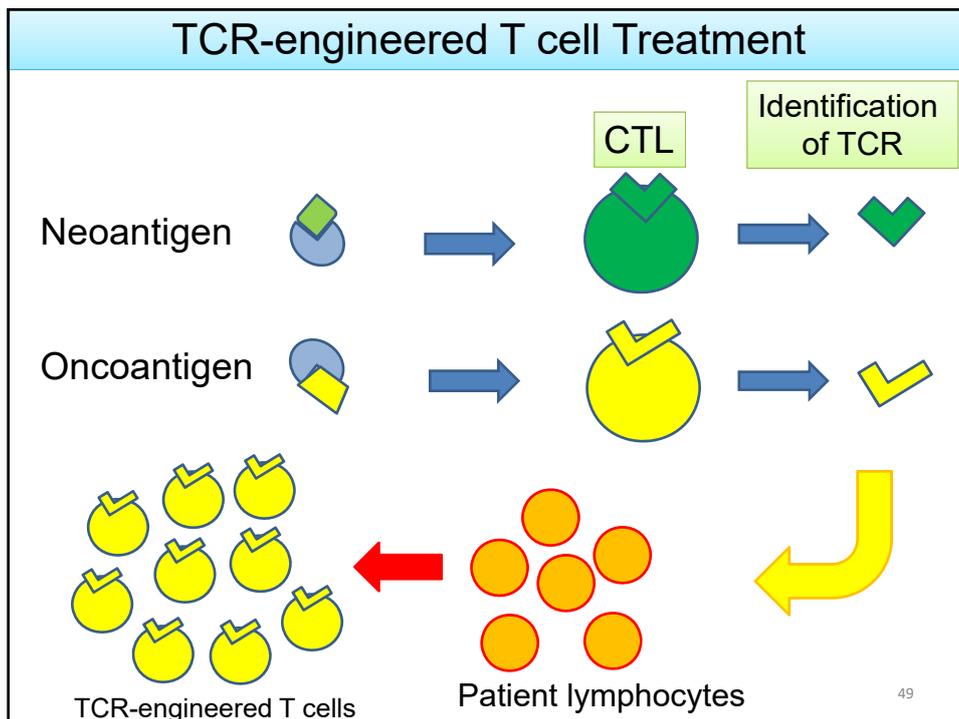
These two clinical trials for glioblastoma provided neoantigens (+over-expressed antigens) just after surgery and subsequent radiation (+chemotherapy).

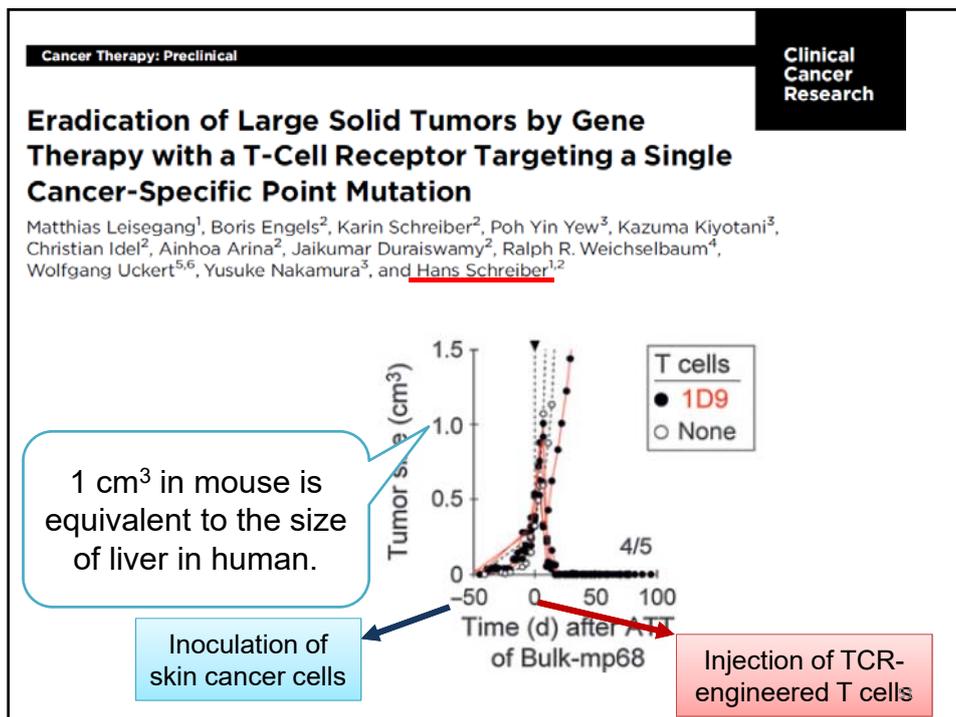
They examined immunological responses and confirmed CTL induction against tumor-specific antigens. Tumor shrinkage was also observed in a subset of patients.

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Manja Idorn^{1,2,3,4}, Jordi Rodon^{5,6,7}, Jordi Piro⁸, Hans S. Foulkes⁹, Ilircha Shalibman¹⁰, Katy McCann¹¹, Regina Mendrzyk¹², Martin Löwer¹³, Monika Stieglbauer^{14,15}, Cedrik M. Britten^{16,17,18}, David Capper^{19,20,21}, Marij L. P. Welters^{22,23}, Juan Sahuquillo²⁴, Katharina Kiesel¹, Evelyn Derhovanessian², Elisa Rusch^{2,3}, Lukas Bunse^{4,7}, Colette Song¹, Sandra Heesch⁷, Claudia Wagner¹, Alexandra Kemmer-Brück², Jörg Ludwig¹, John C. Castle^{2,25}, Oliver Schoor⁷, Arbel D. Tadmor²¹, Edward Green²⁶, Jens Fritsche¹, Miriam Meyer¹, Nina Pawlowski¹, Sonja Dörner¹, Franziska Hoffgaard¹, Bernhard Rössler¹, Dominik Maurer¹, Toni Weltschek¹, Carsten Reinhardt¹, Christoph Huber¹, Hans-Georg Rammensee^{3,4}, Harpreet Singh-Jasuja¹, Ugur Sahin², Pierre-Wes Dietrich¹⁰ & Wolfgang Wick^{6,26}







Thank you for paying your attention!