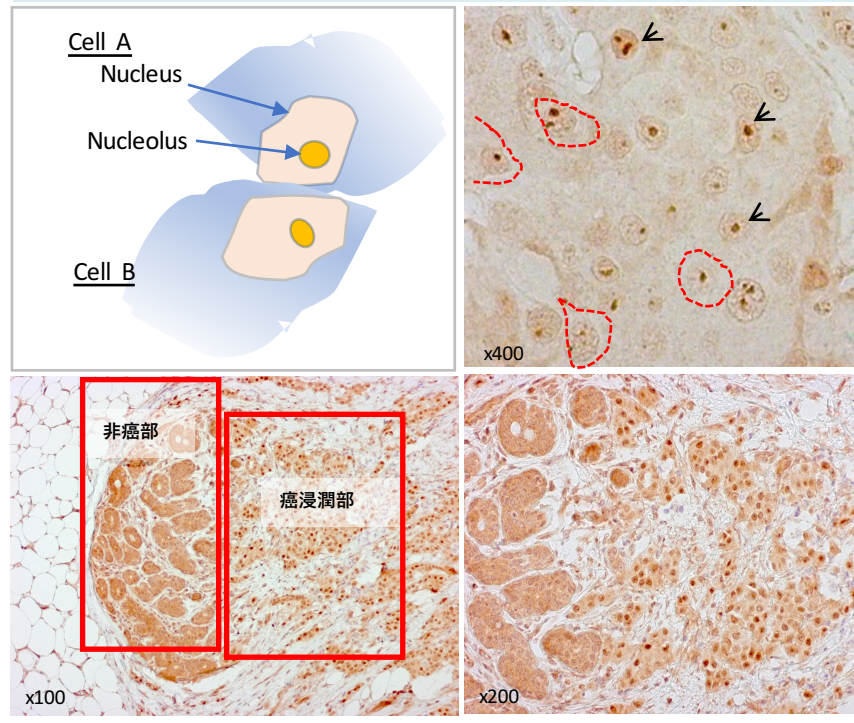


権利化技術 Summary

浸潤性乳管癌

CK2 核小体染色評価による 予後予測指標有効性

Detection of nuclear protein kinase CK2α by immunohistochemical analysis of invasive ductal carcinomas of breast



本手法の手順と結果

- 第1コホート：浸潤性乳管癌術時FFPE試料(n=112)抗CK2抗体-IHC染色実施。再発例(n=12)は核もしくは核小体染色陽性のみへ分類された。CK2核小体陽性群 (全体の30%)の無再発生存期間(RFS)短縮はp StageIIIと Triple-Negative症例で顕著であった。
- CK2核小体染色陽性群は無再発生存期間を規定する唯一の独立変数であり (P = 0.017), 高いハザード比(Hazard R = 5.26)を示した。
- 第2コホート： Luminal type IDC乳癌 症例群(n=59)も同様の結果を得た。早期ステージからも将来の再発リスク群を抽出できることが示された。
- 第3コホート：肺腺癌症例群(n=120)も同様の結果を得て出版した。早期ステージからも将来の再発リスク群を抽出できることが示された。

今後の展望

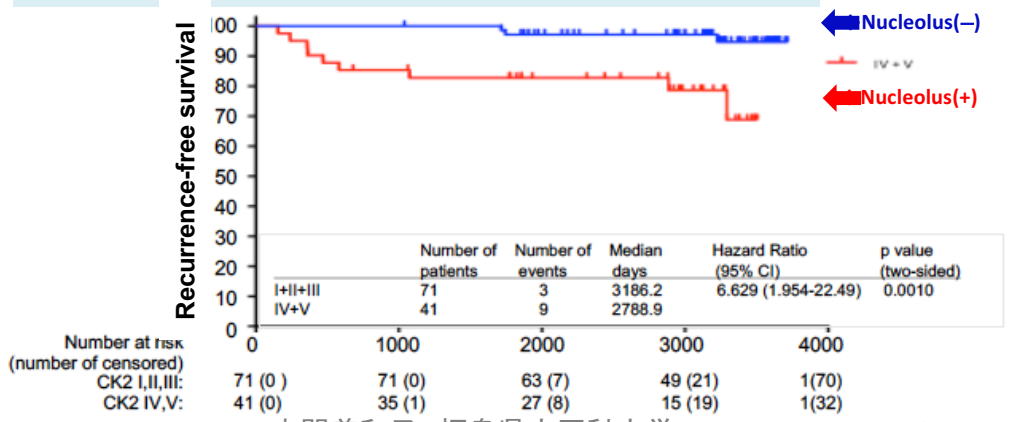
- CK2染色評価を手術直後の臨床病理学的情報へ加えることで, 将来の再発リスク群を早期に評価抽出することで,再発予防への治療を開始できる。
- CK2(旧名称casein kinase 2) 阻害薬の中でFDA治験承認薬CX-4945,他による各種癌を対象とする単剤, 多剤併用, による臨床治験は欧米で進行中である。日本国においてもCK2染色評価と連携する前向き検証等が期待される。

Nucleolar CK2α status as a precise, new, independent prognostic factor

Cox proportional hazards regression / Multivariate				
Factor	Wald	HR	95%-CI	P-value
CK2 Nucleolus (+)	5.711	5.264	1.348-20.553	0.017
Tumor size, >2.0cm	0.639	1.837	0.414-8.152	0.424
p Stage III	0.205	1.356	0.363-5.069	0.651
Nodal lymph, positive	3.616	8.191	0.938-71.56	0.057

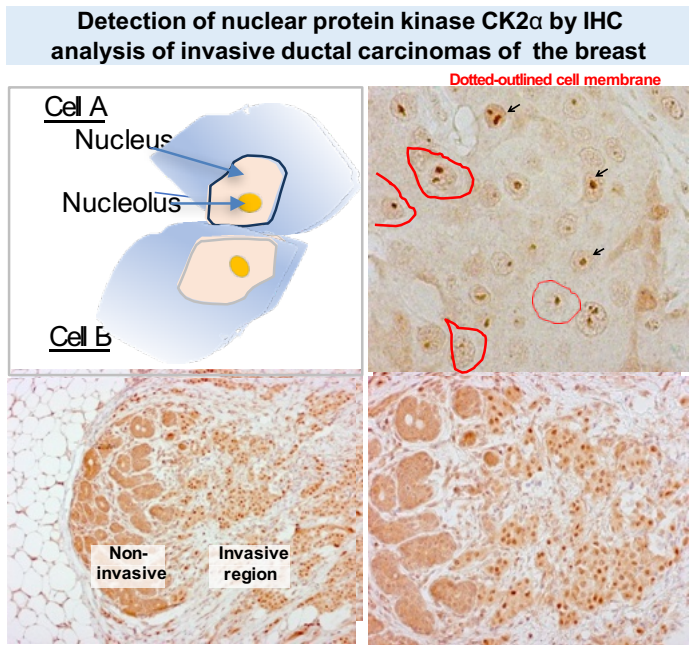
浸潤性乳管癌: Cancer Science 112: 619 (2021)
 乳癌サブタイプ: Lancet Oncology 23: S25 (Abstract, 2022)
 肺腺癌: Oncology Reports 53: 1-9 (2025)
 CK2分子生物学機序: Life Science Alliance 7: e202302077(2024)
 JST新技術動画URL: <https://www.youtube.com/watch?v=yYt51sIRDVk>

Nucleolar CK2α staining is associated with poor outcomes of IDC patients



Patented Technology (JPN)

Nucleolar Localization of Protein Kinase CK2 α as a Prognostic Factor for Breast Cancer



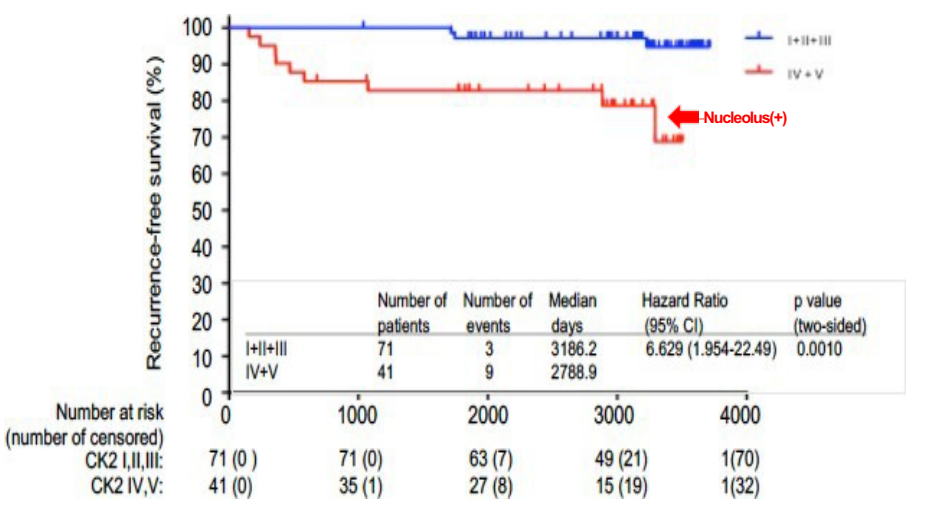
Experimental Protocol and Results

- ✓ We employed CK2 α -IHC staining by FFPE specimens from invasive ductal carcinomas of the breast (n=112) to evaluate the protein levels and subcellular localization.
- ✓ Five categories of CK2 α expression: I, CK2 (-) in the nucleus; II, CK2 (+) in the nucleus; III: CK2 (++) in the nucleus; IV, in the nucleus (+, ++) and nucleolus (+); V, nucleolus (+).

Conclusion and Perspectives:

- ✓ We demonstrated that CK2 α positive IHC staining in **nucleoli** of the breast cancer was strongly associated with tumor recurrence and poor patient outcomes.
- ✓ The results from a statistical platform showed that IHC evaluation of nucleolar CK2 α -positive staining may be a new and independent prognostic factor.
- ✓ The application of this analysis may contribute to the early decision of treatment strategy and to companion diagnostics.
- ✓ Specifically, a more detailed evaluation of CK2 α function in the nucleolar events in malignant cells may lead to the development of novel, more accurately targeted anti-cancer therapeutics.
- ✓ FDA-permitted for clinical trials, **CK2 inhibitor CX-4945** and other CK2is are expected to be approved for utilizing in Japan, in association with this intellectual property.

Nucleolar CK2 α staining is associated with poor outcomes of Invasive ductal carcinomas of the breast

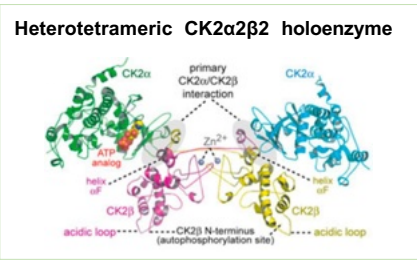


Nucleolar CK2 α status as a precise, new, independent prognostic factor for recurrence-free survival

Cox proportional hazards regression / Multivariate

Factor	Wald	HR	95%-CI	P-value
CK2a Nucleolus (+)	5.711	5.264	1.348-20.553	0.017
Tumor size, >2.0cm	0.636	1.837	0.414-8.152	0.424
p Stage III	0.205	1.356	0.363-5.069	0.651
Nodal lymph, positive	3.616	8.191	0.938-71.56	0.057

CK2a staining	N	Subtotal n(%)	Evaluation	
			Nuclei (+)	Nucleoli (+)
I	7	7 (6.3%)		
II	15	64 (57.1%)		
III	49	105 (93.8%)		
IV	24	41 (36.6%)		41 (93.8%)
V	17			41 (36.6%)



Cancer Science 112: 619-628 2021 by Homma, et al. doi:10.1111/cas.14728
 Lancet Oncology 23: S25 (Abstract) by Homma, et al. doi:10.1016/ s1470-2045(22)00424-72
 Life Science Alliance 7: e202302077 2024 by Homma, et al. doi: 10.26508/lsa.202302077
 Oncology Reports 53: 1-9 2025 by Muto, et al. <https://doi.org/10.3892/or.2024.8837>