Aurora Kinase A (AURKA) is a Predictor of Recurrence in Breast Ductal Carcinoma in situ (DCIS)

Islam Miligy[1,2], Ahmed Gaber[2], Ian O Ellis[1] , Andrew Green[1] and Emad Rakha[1]

[1]Division of Cancer and Stem Cells, School of Medicine, University of Nottingham, Nottingham City Hospital, UK;
[2]Faculty of Medicine, Menoufia University, Egypt

Background and Aims

- Current clinico-pathological parameters are useful predictors of recurrence in breast ductal carcinoma in situ (DCIS), but they are insufficient to reflect its molecular heterogeneity and a proportion of DCIS patients are over-treated.[1] Biological characterisation has the potential for individualising therapy for DCIS.
- Aurora kinases, located on 20q13.2, comprise a family of serine/threonine kinases which play a critical role in regulating mitosis and cytokinesis.[2] We aimed to investigate the role of AURKA in DCIS.

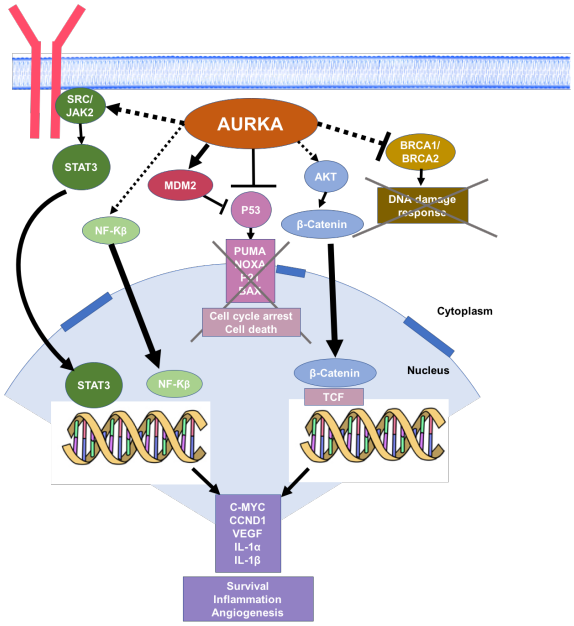

Fig. 1: The role of AURKA in progression of cancer.

Methods

Patients: 776 pure DCIS patients, treated in Nottingham between 1990 and 2012 were included.
Methods: Immunohistochemistry for AURKA was done on the Tissue microarrays (TMAs) constructed from well characterised 776 pure DCIS cohort. Staining was assessed using semi-quantitative histoscore (H-score).
Statistical analysis: Correlations (Pearson Chi Square) with clinico-pathological variables and disease outcome (Kaplan Meier survival) were determined.

Results

- Positive/High AURKA expression was detected in 402 cases, however, 182 cases showed Negative/Low expression (**Fig. 2**).
- Positive/high nuclear expression of AURKA was associated with high nuclear grade, positive ER status and development of local recurrence.

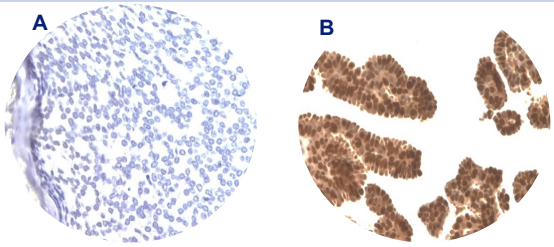

Fig. 2: Expression of AURKA in DCIS, (**A**) Negative and (**B**) Positive.

Survival Analysis

High nuclear expression of AURKA was associated with shorter local recurrence free interval (LRFI) in patients treated with conservative breast surgery (**Fig. 3**).

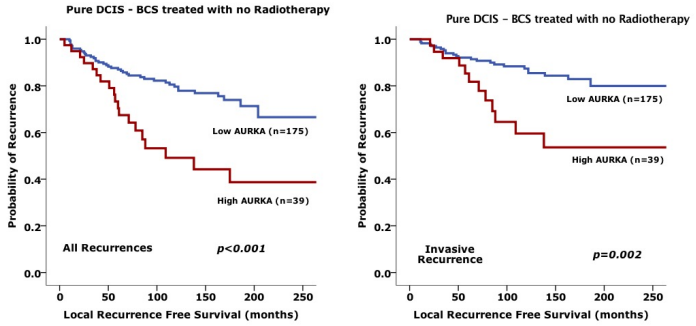

Fig. 3: Association between nuclear expression of AURKA and LRFI.

Multivariate analyses showed that independent predictors of recurrence were high AURKA expression, large DCIS size, high tumour grade and absence of radiotherapy (**Table 1**).

Parameters	Hazard ratio (HR)	95% confidence interval (CI)	p-value
High AURKA expression	3.9	1.7-7.1	**0.001**
DCIS size	3.2	1.1-6.5	**0.045**
DCIS nuclear Grade	4.7	1.1-6.0	**0.040**
Radiotherapy	0.2	0.1-0.8	**0.025**

Table 1: Cox proportional hazard analysis including AURKA.

Conclusion

- AURKA expression predicts local recurrence in DCIS patients and is potentially useful in prognostic stratification of DCIS patients for management decisions.
- AURKA is an oncogenic driver in breast cancer that represents a target for treatment.

References

1- Mori K., et al., Hum Pathol, 2017. S0046-8177(17)30114-4.
*2- Jiang S., et al., Horm Cancer, 2010. **1**(1): 11-20.*