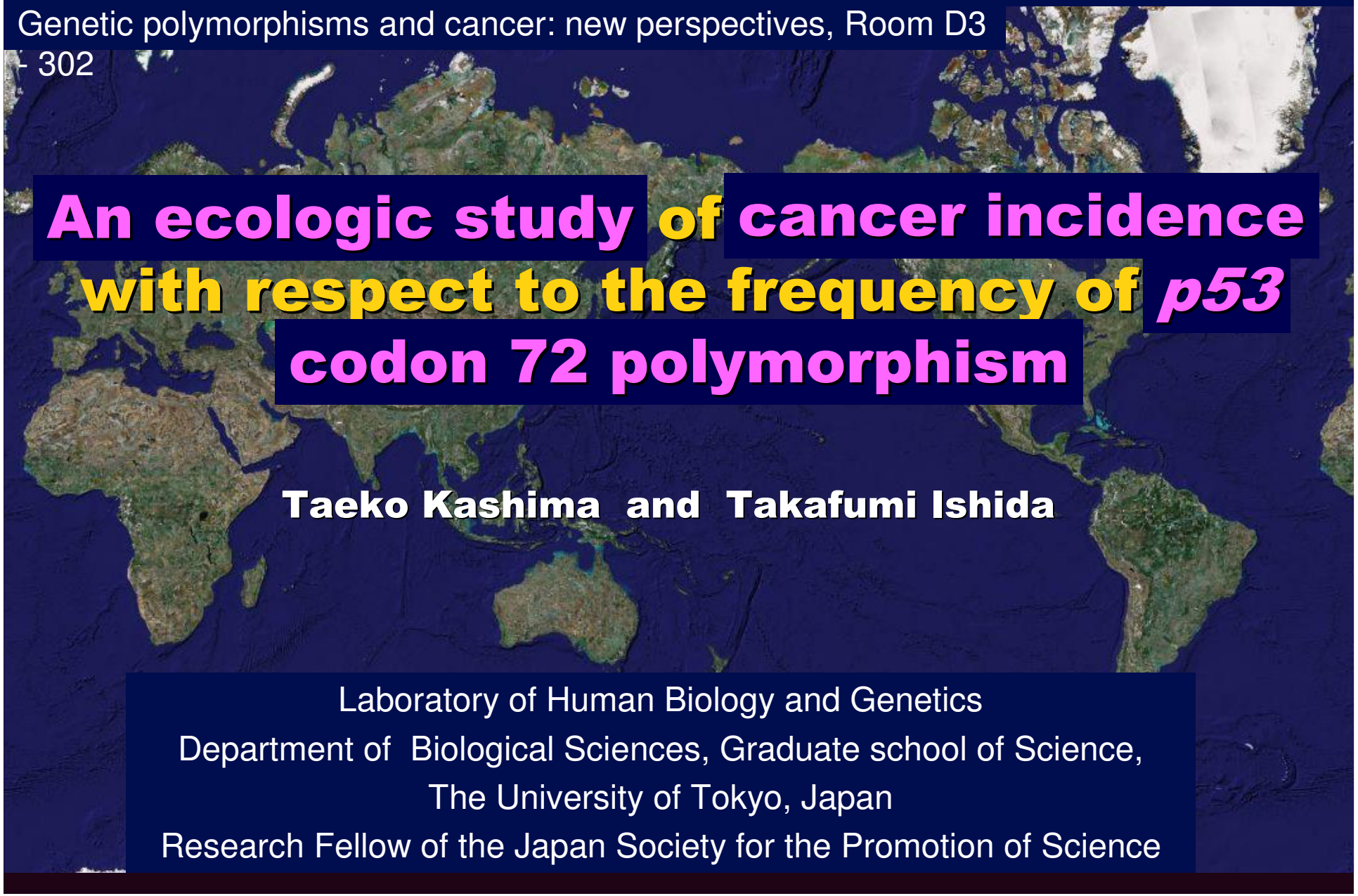
XVIII IEA World Congress of Epidemiology and the VII Brazilian Congress of Epidemiology
Genetic polymorphisms and cancer: new perspectives, Room D3
- 302



An ecologic study of cancer incidence with respect to the frequency of *p53* codon 72 polymorphism

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Cancer incidence

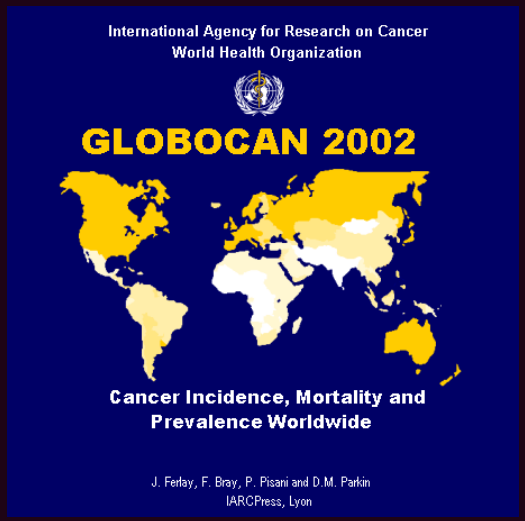
Definition:

The number of new cases arising in a specified age class population in a country as a rate per 100,000 persons-year.

Source:

GLOBOCAN 2002 (IARC)

- This project presents estimates of the incidence from 27 cancers for all countries in the world in 2002.
- The Age-Standardized Rate (ASR, world standard) is calculated using the 5 age-groups 0-14,15-44,45-54,55-64,65+.



This incidence provides an approximation to the average risk of developing a cancer per country.

List of the cancer sites (ICD, 10th revision) 1

Nervous system	
Brain, central nervous system (C70-C72)	
Chest	
Trachea, bronchus and lung (C33+C34)	Thyroid (C73)
Digestive organ	
Mouth (C00-C08)	Nasopharynx (C11)
Other pharynx (C09-C10,C12-C14)	Oesophagus (C15)
Larynx (C32)	Stomach (C16)
Colon and rectum (C18-C21)	Pancreas (C25)
Liver and intrahepatic bile ducts (C22)	
Urinary organs	
Kidney and other and unspecified urinary organs (C64-C66,C68)	Bladder (C67)

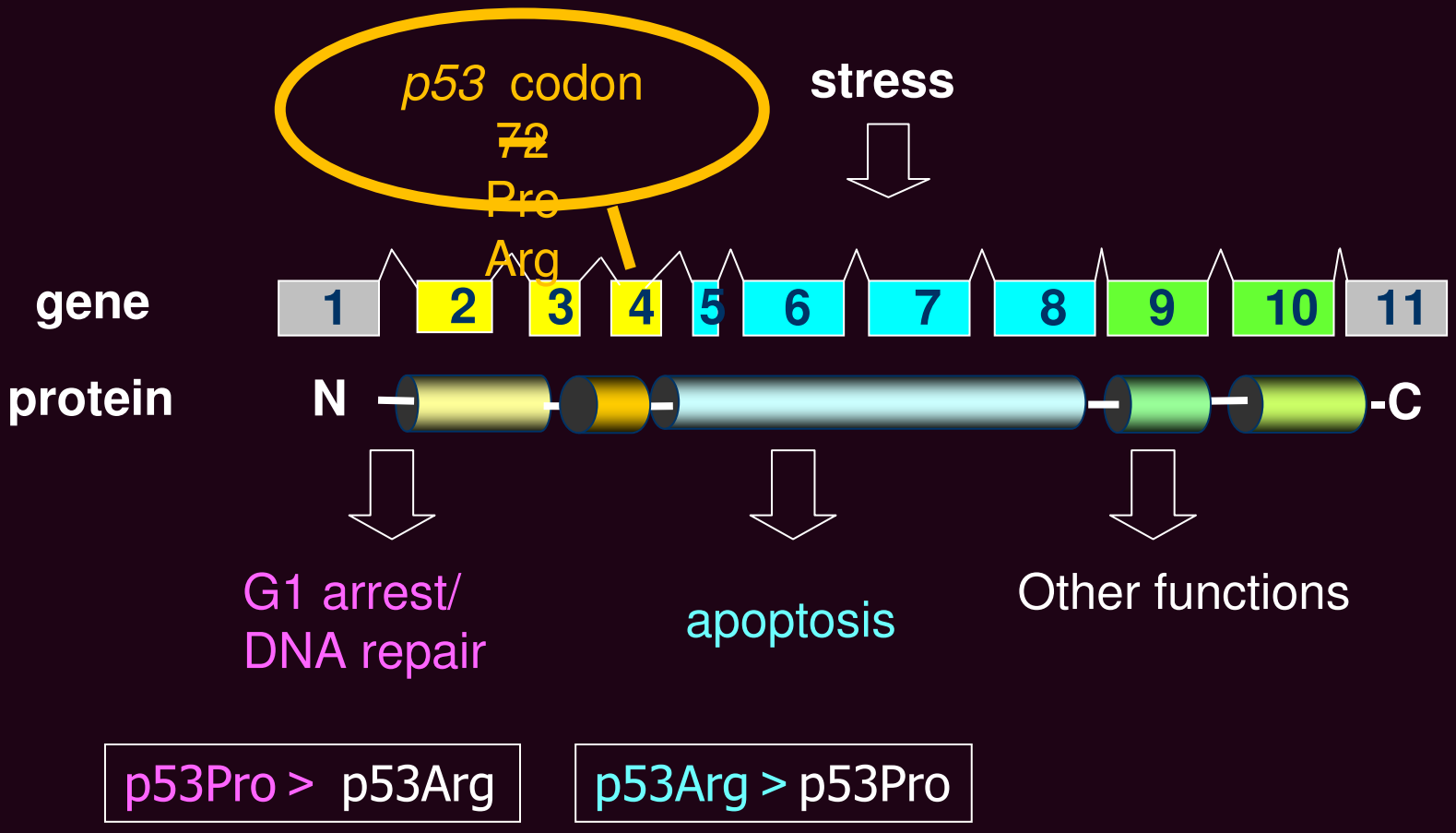
to be continue…

List of the cancer sites (ICD, 10th revision) 2

Male genitals	
Prostate (C61)	Testis (C62)
Female genitals	
Ovary and other uterine adnexa (C56,C57.0-4)	Breast (C50)
Corpus uteri (C54)	Cervix uteri (C53)
Hematogenous & immune system	
Hodgkin lymphoma (C81)	Non-Hodgkin lymphoma (C82-C85,C96)
Leukaemia (C91-C95)	Multiple myeloma (C90)
Others	
Melanoma of skin (C43)	
~~Kaposi sarcoma (C46)~~	
All sites but non-melanoma skin (C00-C96, but C44)	

TP53 TUMOR SUPPRESSOR (*p53*)

maintain genomic stability of a cell in various ways



p53Pro > p53Arg

p53Arg > p53Pro

Epidemiological studies of p53Arg

Case-control studies of p53 codon 72

>600 publications.

contradictory results.

An ecologic study of p53 Arg

It is a useful method to generate some hypothetic idea of etiological importance of p53Arg.

Selection of p53Arg data

Collect p53 codon 72-related papers using PubMed

Search term

(p53 OR tp53) AND (codon 72 OR cod 72 OR cod72 OR position 72 OR arg OR pro OR proline OR arginine OR pro72arg OR arg72pro OR r72p OR p72r OR polymorphisms)

2154 papers

Select and sum up p53Arg data

The inclusion criteria

- studies with non-related subjects
- Use healthy individuals with described ethnicity / general population
- sufficient data to calculate allele frequencies (p53Arg, p53Pro)
- no deviation from Hardy–Weinberg equilibrium for the genotype distribution ($p > 0.01$)
- To exclude double counting in a given population, single paper with largest number was selected

129 papers

Worldwide distribution of p53Arg

44 countries (n = 40040)

Study design

Design: An ecological study (44 countries, 26 cancers)

Aimes: To examine an etiological contribution of p53 codon 72 variants in the worldwide cancer incidence.

Resource:

p53Arg genotype frequencies	129 Publications (Pub Med)
incidence of Cancers	GLOBOCAN 2002
Socioecological factor (1st principle of 1 and 2)	
1. GNP (per capita)	WHOSIS
2. Consumption quantity of Animal products (kcal/capita/day)	FAOSTAT

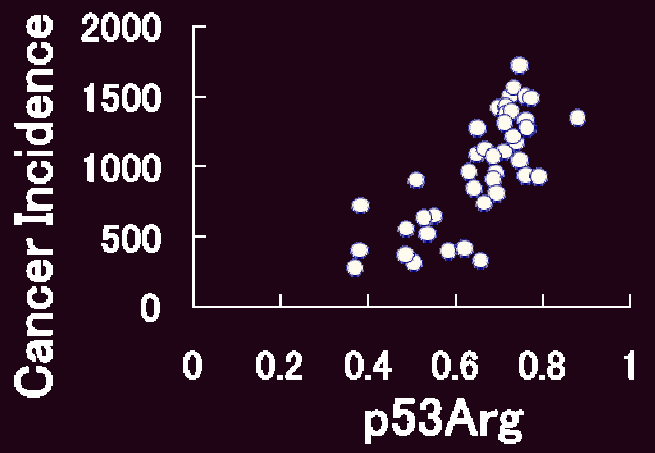
Significance of the statistics:

Spearman's $\rho > 0.4$ (middle), $\rho > 0.7$ (high)

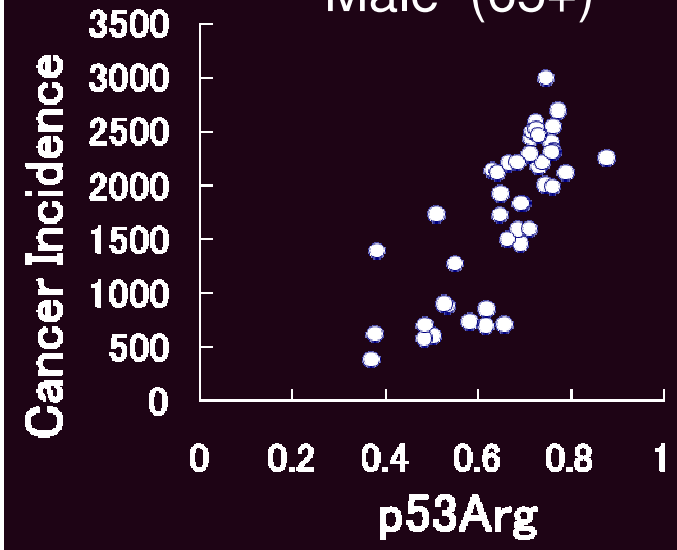
P value < 0.05

All sites but non-melanoma skin (C00-C96, except C44)

Female (65+)



Male (65+)



Spearman's ρ

p53Arg	15-44	45-55	54-64	65+
Female	0.72	0.68	0.75	0.77
Male	0.70	0.53	0.67	0.81

Socioecological factor	15-44	45-55	54-64	65+
Female	0.78	0.75	0.79	0.77
Male	0.72	0.52	0.65	0.86

⇩ (p53Arg + Socioecological factor)

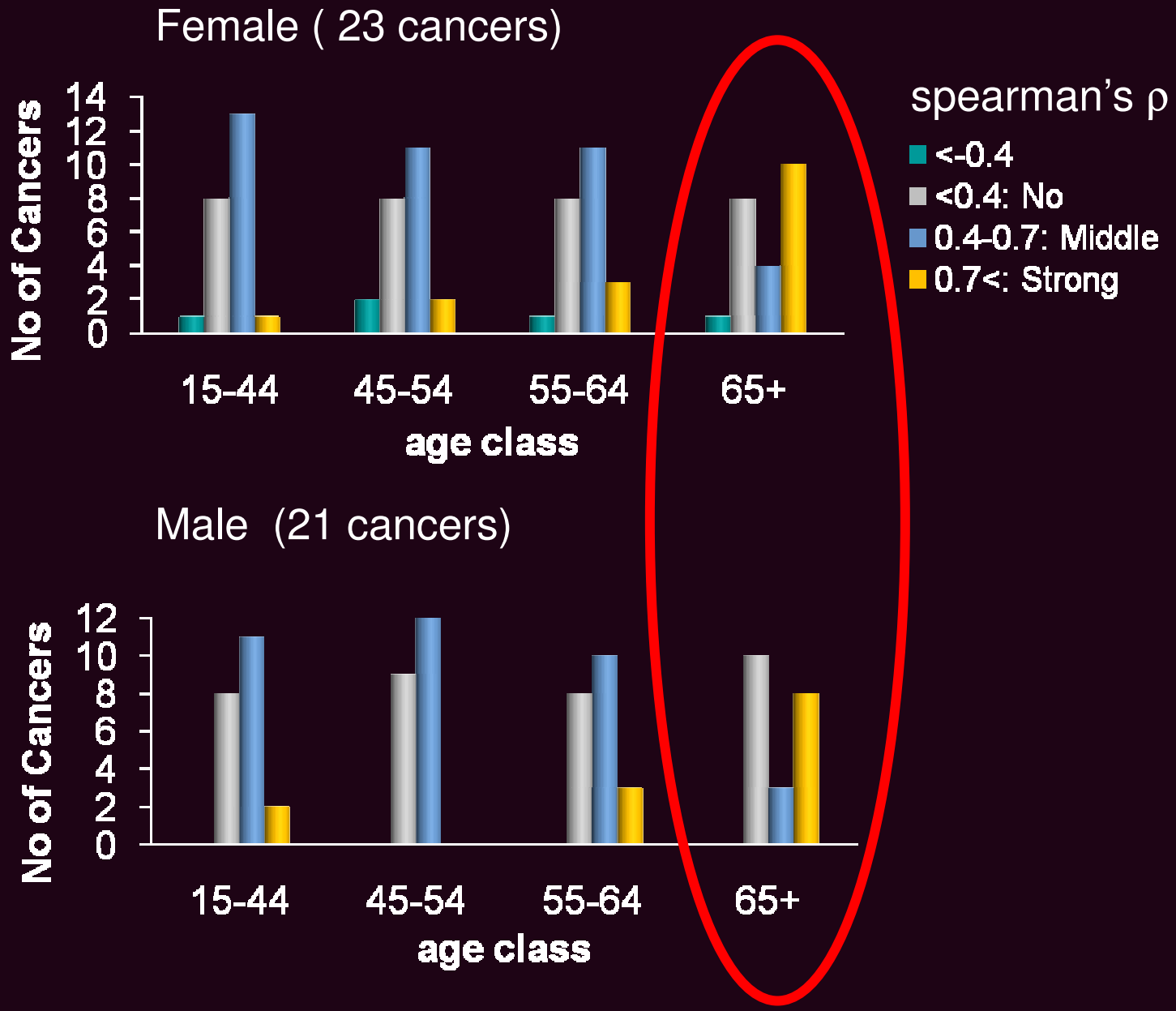
	15-44	45-55	54-64	65+
Female	0.78	0.76	0.84	0.83
Male	0.72	0.54	0.69	0.89

Functional differences between p53Arg and p53Pro

	p53Arg	p53Pro
Induction of apoptosis	High	Moderate
Interaction with transcriptional machinery	Low	High
Transactivation	Moderate	Higher
Dysfunction by p53 somatic mutation	Sensitive	Resistant
Dysfunction with senescence	Sensitive	Resistant

p53 functions may be associated with cancer incidence

Tendency of correlation among cancers



Melanoma of skin (C43)

Spearman's ρ

	15-44	45-55	54-64	65+	ASR
Female	0.75	0.73	0.78	0.78	0.77
Male	0.80	0.69	0.70	0.74	0.75

(p53Arg + Socioecological factor)

	15-44	45-55	54-64	65+	ASR
Female	0.81	0.79	0.81	0.84	0.82
Male	0.85	0.74	0.75	0.78	0.80

Pattern of correlation varied by cancers.

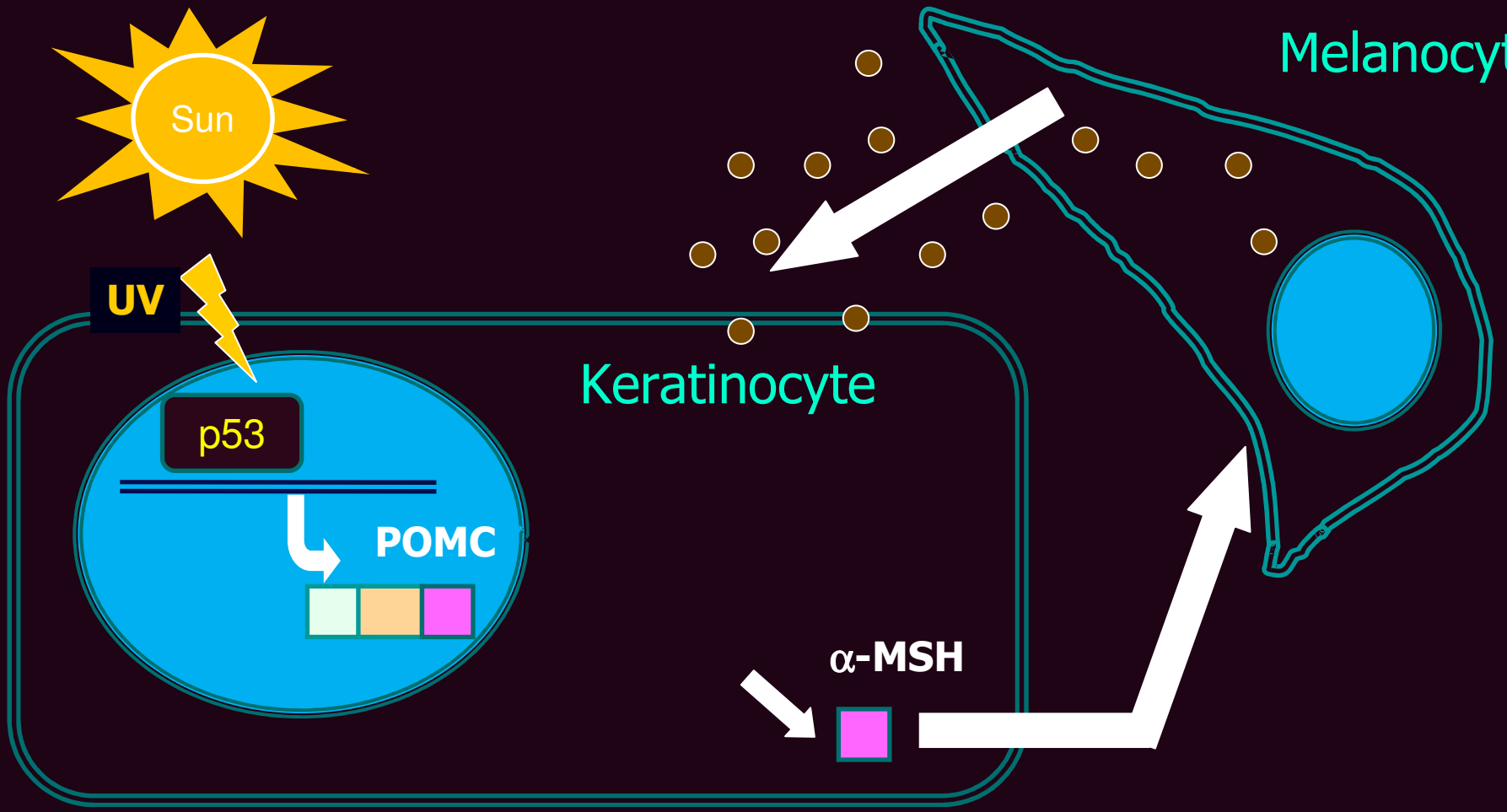
p53 function maintaining genomic stability

&

other p53 functions

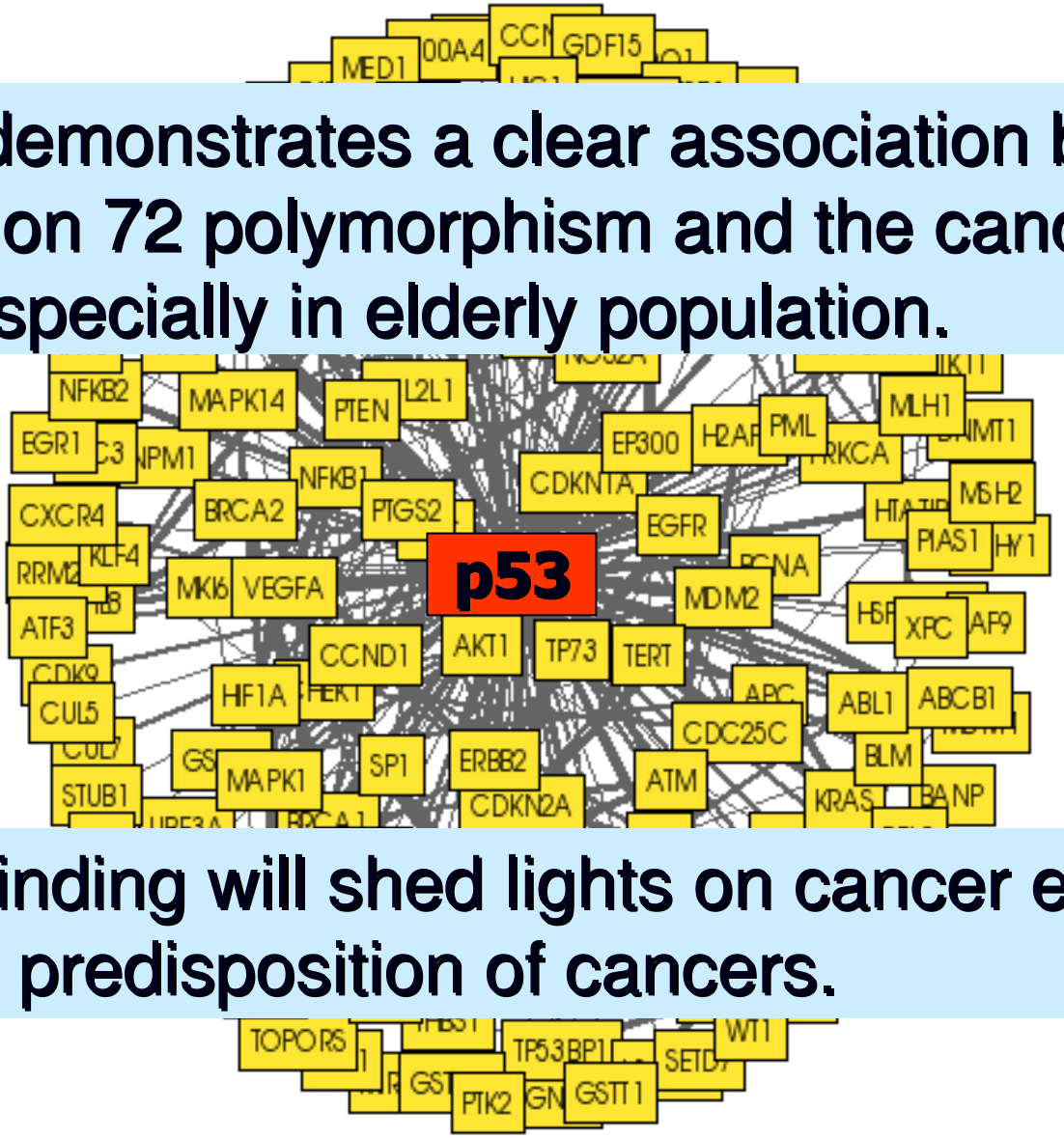
can be related to cancer development.

p53 regulates Suntan response.



Conclusion

This study demonstrates a clear association between the *p53* codon 72 polymorphism and the cancer incidence especially in elderly population.



This novel finding will shed lights on cancer etiology and genetic predisposition of cancers.

http://www.bioportal.jp/