Teacher's Guide to Microarray Exercise

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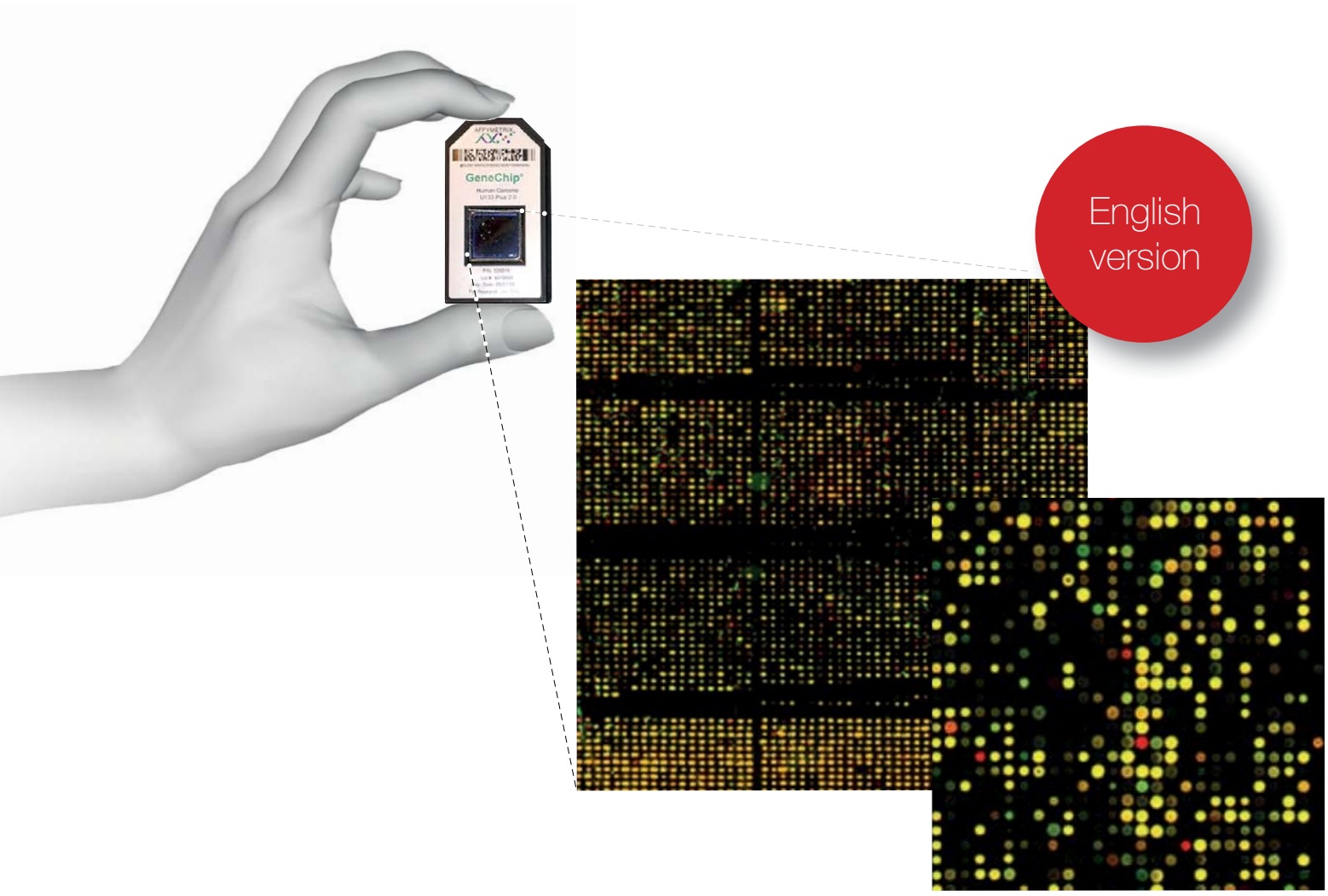
Version 2.3



English version

ELLS – European Learning Laboratory for the Life Sciences

EMBL

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As sequencing of the human genome is helping to move research out of the laboratory into the clinic, it is tempting to make bold assessments as to where genetic applications may take us in the long run.

Now that you understand the science behind DNA chips, we are going to look at an exercise that illustrates just how powerful this technology can be.

A Real-Life Story of Cancer Diagnosis

This exercise has been adapted from "Snapshots of Science & Medicine, Teacher's Guide: DNA Chips" published by the NIH Office of Science and Education and Office of Research on Women's Health. More information can be found at: http://science-education.nih.gov/snapshots.

Cancer is caused by damage to the genes that control cell division. As a result of this damage cells divide uncontrollably. Cancer cells have different gene expression patterns from normal cells, and different types of cancer cells show different patterns.

In 1999, a team of scientists in America used DNA microarrays to distinguish between two clinically similar types of cancer: **a**cute **l**ymphoblastic **l**eukaemia (**ALL**), and **a**cute **m**yelogenic **l**eukaemia (**AML**), which both affect cells in the bone marrow. They were able to identify a set of 50 genes that show differences in activities between the two cancer types.

In the following exercise, we are going to use some of these genes in a small microarray to show how microarrays can be used to diagnose patients with these cancer types. The following table gives you a summary of the genes used in this microarray, as well as in which types of cancer these genes show high activity.

Location	Gene Name	Gene highly active
A1	Zyxin	AML
A2	Cyclin D3	ALL
A3	Myosin light chain	ALL
A4	HOX A-9	AML
A5	SNF 2 A	ALL
B1	Coenzyme A	ALL
B2	Leptin receptor	AML
B3	OP 18	ALL
B4	Dynein light chain	Neither (control)
B5	SRP9	ALL
C1	Actin	Both (control)
C2	IL7 receptor-33	ALL
C3	CD-33	AML
C4	MCM 3	ALL
C5	LYN	AML
D1	Myc 3	Neither (control)
D2	ATPase	AML
D3	SRP9	AML
D4	CD 19	Neither (control)
D5	Catalase	AML
E1	IL8 receptor	AML
E2	Lysozyme	AML
E3	Topoisomerase II	ALL
E4	Acyl-CoA dehydrogenase	ALL
E5	Glucose-6-phosphate	Both (control)

The genes that are termed controls are genes that are either expressed in both or neither of the cancer types. These genes do not provide any information about the cancer type, but are usually included in microarrays to show that nothing has gone wrong during the experiment.

mRNA was extracted from cells of three different patients, A, B and C, labelled with fluorescent markers and used to perform hybridizations. For reasons of simplicity, only the genes that were active during the experiment are shown in the next three tables.

Can you make a diagnosis for the three different patients?

	1	2	3	4	5
A		*	*		
B	*		*		
C	*			*	
D					
E			*		*

Microarray results for patient A

	1	2	3	4	5
A				*	
B		*			
C	*				
D					
E					*

Microarray results for patient B

	1	2	3	4	5
A	*			*	
B		*			
C	*		*		
D		*	*		
E					*

Microarray results for patient C

Patient A has 5 genes (A2, A3, B1, B3, C4) that are highly active in ALL, whereas the other genes are controls (they do not provide any information about the type of cancer). We could therefore say that this patient has ALL.

Patient B has two genes (A4, B2) that are highly expressed in AML, whereas the other genes indicate controls. Diagnosing this patient with AML is quite risky. This patient does not have any other genes active in AML cells. The high activity of these genes could be due to another cancer type, different from ALL and AML. As a result, this patient cannot be diagnosed as either AML or ALL positive.

Patient C has 6 genes (A1, A4, B2, C3, D2, D3) that are highly active in AML cells. The remaining genes in the array are controls. Patient C probably has AML.

Note: In the future, by simply looking at different activities of genes on microarrays, doctors will be able to make an accurate prediction of the cause or type of a patient’s disease, which will help them to tailor treatments to the individual. Such methods are also described in the Reading Club section.

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