

WALLACE-CROSS/PASAHOW

14 1 HAVE A DIFFERENCE BETWEEN YOUR PRIMER SEQUENCE AND THE SEQUENCE
2 YOU WERE LOOKING FOR AND THAT SOME DIFFERENCES AT LEAST WOULD
3 STOP YOU FROM DOING PCR.

4 A. WELL, THE PATENT SAID THAT IF YOU HAD DIFFERENCES, YOU'D
5 GET -- YOU COULD GET PCR. I DIDN'T . . . WE KNEW THAT IF YOU
6 HAD DIFFERENCES, YOU COULD GET PRIMER EXTENSION.

7 THIS (INDICATING) WAS SURPRISING TO ME.

8 Q. YOU THINK YOU WERE THE FIRST PERSON TO -- TO DISCOVER THAT A
9 DIFFERENCE AT THE END OF THE PRIMER PREVENTED PCR FROM WORKING?

10 A. THAT'S WHAT WE THOUGHT.

11 (PAUSE IN PROCEEDINGS)

12 Q. (BY MR. PASAHOW) NOW, IN THIS PATENT, YOU HAVE A BACKGROUND
13 SECTION, AS PATENTS DO.

14 (PAUSE IN PROCEEDINGS)

15 Q. (BY MR. PASAHOW) AND IN THAT SECTION, YOU REVIEW SOME OF
16 THE ART FROM THE PAST THAT HAD INVOLVED PROBING; IS THAT RIGHT?

17 A. WHICH PAGE ARE YOU LOOKING AT?

18 Q. AT THE BOTTOM OF PAGE 1 OF THE APPLICATION.

19 YOU HAVE A REFERENCE THERE TO THE ARTICLE YOU WENT OVER
20 WITH MR. FIGG, THE CONNER ARTICLE.

21 A. THAT'S TRUE.

22 Q. AND YOU SAY: "CONNER DESCRIBED A MORE GENERAL APPROACH
23 TO THE DIRECT DETECTION OF SINGLE NUCLEOTIDE VARIATION
24 BY THE USE OF ALLELE-SPECIFIC OLIGONUCLEOTIDE
25 HYBRIDIZATION."

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14 1 A. THAT'S TRUE.

2 Q. AND WHAT THAT MEANS IS THAT YOUR ARTICLE -- THE ARTICLE YOU
3 AND DR. CONNER AND OTHERS WROTE DESCRIBED USING PROBES THAT HAD
4 SEQUENCES TO DETECT THE DNA; IS THAT RIGHT?

5 A. THAT'S TRUE.

6 Q. AND THAT WAS EXACTLY THE PROCESS THAT YOU DESCRIBED DURING
7 YOUR TESTIMONY WITH MR. FIGG.

8 A. THE HYBRIDIZATION PROCESS? YES.

9 Q. YES.

10 AND YOU EXPLAINED A BIT MORE ABOUT THAT PROCESS, AND
11 THEN YOU START TO TALK ABOUT PCR.

12 AND YOU SAY: "ALL OF THE ABOVE APPROACHES ARE
13 TECHNICALLY CHALLENGING, REQUIRE A REASONABLY LARGE
14 AMOUNT OF DNA, AND ARE NOT VERY RAPID. THE POLYMERASE
15 CHAIN REACTION (PCR) DEVELOPED BY SAIKI, ET AL.,
16 PROVIDED A METHOD TO RAPIDLY AMPLIFY SMALL AMOUNT OF A
17 PARTICULAR TARGET DNA."

18 A. (NODDING HEAD.)

19 Q. IS ALL OF THAT CORRECT?

20 A. WELL, AT THE TIME, I DIDN'T KNOW ABOUT THE KHORANA PRIOR
21 ART, AND . . . DIDN'T -- SO GAVE CREDIT TO SAIKI, ET AL., AS THE
22 DEVELOPER OF PCR, YES.

23 AND IT WAS -- IT IS TRUE THAT PCR COULD AMPLIFY DNA,
24 AND THAT LEFT THE LIMITATION, WHICH WAS THE SPECIFICITY.

25 Q. AND YOU TOLD US IN THAT OTHER PIECE WE LOOKED FOR THAT PCR

WALLACE-CROSS/PASAHOW

14 1 WAS A DRAMATIC IMPROVEMENT IN THE SENSITIVITY OF THESE PROCESSES
2 THAT YOU HAD WORKED OUT AS WELL.

3 A. OH, NOT ONLY WAS; IT IS.

4 Q. SO PCR MADE IT DRAMATICALLY MORE SENSITIVE; IT MADE IT LESS
5 TECHNICALLY CHALLENGING; IT MADE IT SO YOU COULD USE LESS DNA;
6 AND IT MADE IT MORE RAPID; IS THAT RIGHT?

7 A. THAT'S TRUE.

8 Q. AND THAT WOULD HAVE BEEN OF USE TO YOU IN 1984 IF YOU HAD
9 THOUGHT OF IT IN CONNECTION WITH YOUR WORK.

10 A. YES. IT PROBABLY WOULD HAVE BEEN, YES.

11 Q. NOW, WHEN YOU WERE IN GRADUATE SCHOOL, DIDN'T YOU STUDY
12 THE -- THE WORK THAT DR. KHORANA DID?

13 A. I STUDIED DR. KHORANA'S WORK, BUT I'M NOT ABSOLUTELY CERTAIN
14 I EVER READ THE KLEPPE PAPER AT THAT TIME.

15 Q. YOU JUST CAN'T RECALL WHETHER YOU READ IT OR NOT?

16 A. NO.

17 Q. THOSE PAPERS WERE PART OF THE ORDINARY GRADUATE EDUCATION OF
18 SOMEONE IN YOUR FIELD; ISN'T THAT RIGHT?

19 A. (NODDING HEAD.) BUT I WAS A STUDENT, AN UNDERGRADUATE
20 STUDENT BEFORE THAT TIME, AND A GRADUATE STUDENT JUST AT THAT
21 TIME I STARTED GRADUATE SCHOOL IN '71, SO --

22 Q. BUT LOTS OF -- I'M SORRY.

23 A. WELL, DOCTOR -- FOR EXAMPLE, DR. KORNBERG TESTIFIED THAT I
24 THINK, FOR HIS BOOK, HE READ 10,000 ARTICLES.

25 Q. UH-HUH.

WALLACE-CROSS/PASAHOW

14 1 A. I'M NOT ABSOLUTELY CERTAIN THAT I'VE READ ALL THE SAME
2 10,000 ARTICLES.

15 3 Q. UH-HUH. BUT DURING YOUR GRADUATE SCHOOL, YOU CERTAINLY
4 BECAME FAMILIAR WITH DR. KHORANA'S ART.

5 A. THAT'S TRUE.

6 Q. AND YOU CERTAINLY BECAME FAMILIAR WITH DR. KORNBERG'S BASIC
7 PRINCIPLES OF PRIMER EXTENSION.

8 A. THAT'S TRUE.

9 Q. AS WAS TRUE OF A LOT OF PEOPLE IN YOUR FIELD.

10 A. THAT'S TRUE.

11 (PAUSE IN PROCEEDINGS)

12 Q. (BY MR. PASAHOW) IN CONNECTION WITH THIS PATENT THAT WE'VE
13 BEEN LOOKING AT, THE ALLELE-SPECIFIC PCR PATENT, AND IN
14 CONNECTION WITH YOUR OBLIGATION TO SUPPLY THE PATENT OFFICE WITH
15 THE MATERIAL RELEVANT REFERENCES, DID YOU SUPPLY THE PATENT
16 OFFICE WITH A COPY OF ANY OF THE KHORANA REFERENCES?

17 A. NO. I WAS UNAWARE OF THEM.

18 Q. DID YOU SUPPLY THE PATENT OFFICE WITH A COPY OF THE TWO HONG
19 ARTICLES YOU TOLD US ABOUT YESTERDAY (SIC)?

20 A. NO, I DID NOT.

21 Q. DID YOU SUPPLY THE PATENT OFFICE WITH A COPY OF THE ARTICLE
22 THAT YOU TOLD US ABOUT YESTERDAY (SIC) THAT YOU WROTE CONCERNING
23 SEQUENCING WITH DOUBLE-STRANDED TEMPLATES?

24 A. NO. I FIGURED THAT PRIOR ART'S WELL DESCRIBED BY THE SAIKI
25 REFERENCE. I MEAN, NOT NECESSARILY MORE RELEVANT.

WALLACE-CROSS/PASAHOW

15 1 Q. YOU THOUGHT THAT THOSE ARTICLES ARE DESCRIBED IN THE SAIKI
2 REFERENCE?

3 A. THOSE ARTICLES DESCRIBE THE SAME PROCESS THAT SAIKI
4 DESCRIBED. I MEAN, I MEANT THE KHORANA PRIOR ART, BUT I DIDN'T
5 KNOW ABOUT THEM.

6 Q. THE HONG ARTICLE IS NOT DESCRIBED IN THE --

7 A. OH, BUT THAT'S PRIMER EXTENSION. THAT'S EVERYDAY STUFF.
8 EVERYBODY WAS DOING DNA SEQUENCING AT --

9 Q. LET ME FINISH MY QUESTION IF I MIGHT:

10 THE HONG ARTICLE IS NOT DESCRIBED IN THE SAIKI ARTICLE.

11 A. NO.

12 Q. AND YOUR DOUBLE-STRANDED SEQUENCING ARTICLE IS NOT DESCRIBED
13 IN THE SAIKI ARTICLE.

14 A. NO, I GUESS NOT.

15 (PAUSE IN PROCEEDINGS)

16 Q. (BY MR. PASAHOW) LET ME SHOW YOU ONE OTHER PATENT OF YOURS.
17 IT'S BEEN MARKED AS EXHIBIT B-186. IT'S SERIAL NUMBER 402,450.

18 A. (WITNESS EXAMINES DOCUMENT.) YES.

19 Q. YOU ARE ONE OF THE INVENTORS ON THIS PATENT?

20 A. YES.

21 Q. AND YOU EXECUTED THE OATH TO THE PATENT OFFICE AT THE END OF
22 OCTOBER 1989; IS THAT RIGHT?

23 A. UH-HUH. YES.

24 Q. IN THIS PATENT, DO YOU TELL THE PATENT OFFICE ABOUT THE
25 KHORANA REFERENCES?

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15

1 A. NO. I THINK WE . . . USED THE . . . '195 AND '202
2 REFERENCES.

3 Q. AND BY THAT, YOU MEAN YOU TOLD THE PATENT OFFICE ABOUT THE
4 CETUS PATENTS.

5 A. I DIDN'T KNOW ABOUT THE OTHER ONES.

6 Q. WELL, ISN'T IT TRUE THAT THIS WAS FILED AFTER DU PONT HAD
7 FILED THIS LAWSUIT?

8 A. I DON'T KNOW WHEN DU PONT FILED THE LAWSUIT.

9 Q. BUT YOU SATISFIED YOUR OBLIGATION TO PROVIDE THE MATERIAL
10 PRIOR ART TO THE PATENT OFFICE HERE BY CITING TO THE CETUS
11 PATENT AND WHAT IT CONTAINED; IS THAT RIGHT?

12 A. THAT WAS WHAT WE DID AT THAT TIME, YEAH.

13 Q. HAVE YOU SINCE SUPPLIED THE KHORANA REFERENCES TO THE PATENT
14 OFFICE IN CONNECTION WITH THAT APPLICATION?

15 A. I DON'T KNOW IF MR. IRONS, OUR ATTORNEY, HAS DONE THAT.

16 Q. DID YOU ASK THAT IT BE DONE?

17 A. NO, I HAVE NOT.

18 (PAUSE IN PROCEEDINGS)

19 Q. (BY MR. PASAHOW) LET'S LOOK TO A DIFFERENT SUBJECT.
20 INSTEAD OF LOOKING AT WHAT -- WHAT WAS SAID TO THE PATENT
21 OFFICE, LET'S LOOK AT WHAT YOU PUBLISHED IN SOME ARTICLES.

22 DO YOU STILL HAVE THE ARTICLE THAT I SHOWED YOU WHICH
23 WAS MARKED AS B-149 UP THERE?

24 A. (WITNESS SEARCHES THROUGH DOCUMENTS.) B-149?

25 Q. PERHAPS I DIDN'T GIVE IT TO YOU.

WALLACE-CROSS/PASAHOW

15 1 A. WHICH ONE IS IT?

2 (PAUSE IN PROCEEDINGS)

3 Q. (BY MR. PASAHOW) I'M SORRY. MY MISTAKE. LET ME SHOW YOU
4 WHAT WE'VE MARKED AS EXHIBIT B-149.

5 A. (WITNESS EXAMINES DOCUMENT.) YES, THAT'S A PAPER I
6 PUBLISHED.

7 Q. AND YOU ARE WHAT'S CALLED THE SENIOR AUTHOR ON IT?

8 A. THAT'S CORRECT.

9 Q. AND IT WAS PUBLISHED WITH A NUMBER OF OTHER SCIENTISTS IN
10 APRIL 1989; IS THAT RIGHT?

11 A. YES.

12 Q. AND IT SAYS IT'S PUBLISHED IN A -- A JOURNAL CALLED THE
13 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA.

14 WHAT IS THAT?

15 A. THE NATIONAL ACADEMY OF SCIENCE IS AN ORGANIZATION OF
16 SCIENTISTS, WELL-RESPECTED SCIENTISTS, AND THEY PUBLISH A
17 JOURNAL, A SCIENTIFIC JOURNAL. AND YOU CAN PUBLISH YOUR WORK IN
18 THAT JOURNAL. IT'S A WIDELY-READ JOURNAL.

19 Q. NOW, HERE, IN EXPLAINING THE BACKGROUND OF THE WORK YOU DID,
20 YOU DESCRIBE THE PCR REACTION; IS CORRECT?

21 (PAUSE IN PROCEEDINGS)

22 THE WITNESS: RIGHT.

23 Q. (BY MR. PASAHOW) YOU BEGIN BY EXPLAINING THE ARTICLE YOU
24 AND DR. CONNER WROTE.

25 AND THEN YOU GO ON TO SAY ABOUT THAT METHOD AND THE

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15 1 OTHERS:

2 "ALL OF THE ABOVE WERE MORE TECHNICALLY
3 CHALLENGING, REQUIRED A REASONABLY LARGE AMOUNT OF
4 DNA, AND ARE NOT VERY RAPID."

5 A. RIGHT.

6 Q. SAME SORT OF THINGS YOU TOLD THE PATENT OFFICE.

7 AND THEN YOU WENT ON TO SAY: "THE POLYMERASE
8 CHAIN REACTION DEVELOPED BY SAIKI, ET AL., PROVIDED A
9 METHOD TO RAPIDLY AMPLIFY SMALL AMOUNTS OF A
10 PARTICULAR TARGET DNA."

11 AND SAIKI, ET AL., OF COURSE, IS A REFERENCE TO THE
12 ARTICLE BY THE CETUS SCIENTISTS IN DECEMBER 1985; IS THAT RIGHT?

13 A. THAT'S CORRECT.

14 (PAUSE IN PROCEEDINGS)

15 Q. (BY MR. PASAHOW) IF YOU HAD WANTED TO FIND THE KHORANA ART
16 THAT YOU DISCUSSED WITH MR. FIGG, THESE -- THESE ARTICLES THAT
17 WERE PUBLISHED FROM HIS LABORATORY, DID YOU HAVE A MECHANISM
18 TO -- TO DO IT?

19 A. MY NORMAL MECHANISM -- YOU CAN SEARCH COMPUTER DATABASES.

20 Q. UH-HUH.

21 A. THE NORMAL MECHANISM IS OFTEN TO RELY ON OTHER PREVIOUS
22 PUBLICATIONS, SO I WAS RELYING ON THE SAIKI ARTICLE, FOR
23 EXAMPLE, IN THIS CASE, AS MY BASIS FOR THE -- FOR WHAT OTHERS
24 HAVE DONE. THEY DIDN'T DESCRIBE KLEPPE, FOR SOME REASON.

25 Q. WELL, YOU WERE VERY FAMILIAR WITH THE BACKGROUND ART

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16 1 BECAUSE, IN 1984, YOU HAD WRITTEN THAT MAJOR REVIEW OF ALL THAT
2 ART; ISN'T THAT RIGHT?

3 A. I HAD REVIEWED THE AREA OF USE OF SYNTHETIC DNA, YES.

4 Q. YES.

5 A. SYNTHESIS AND USE OF SYNTHETIC DNA.

6 Q. AND YOU --

7 A. WE LOOKED AT 137 REFERENCES, I THINK IT WAS, IN THAT PAPER.

8 Q. INCLUDING SEVERAL FROM DR. KHORANA'S LABORATORY.

9 A. YES.

10 Q. AND IF YOU HAD WANTED TO FIND ANY PARTICULAR REFERENCE FROM
11 DR. KHORANA'S LABORATORY, YOU COULD HAVE USED A COMPUTER TO DO
12 THAT AT THE TIME YOU WROTE THIS ARTICLE.

13 A. THAT'S TRUE, IF I WANTED TO LOOK FOR DR. KHORANA'S WORK, I
14 COULD HAVE.

15 Q. AND THAT COMPUTER WOULD HAVE HELPED YOU FOCUS IN ON THE
16 PARTICULAR ARTICLES YOU WANTED?

17 A. YES, IT WOULD HAVE.

18 Q. AND YOU HAD THAT AT THE TIME YOU WROTE YOUR REVIEW ARTICLE
19 AS WELL.

20 A. I DON'T KNOW. I PROBABLY USED OUR LIBRARY SERVICE FOR THAT,
21 YES.

22 (PAUSE IN PROCEEDINGS)

23 THE WITNESS: THAT WAS IN 1984. I DON'T REMEMBER.

24 Q. (BY MR. PASAHOW) NOW, AFTER YOU PUBLISHED THIS CONNER
25 ARTICLE THAT WE'VE BEEN TALKING ABOUT, WHICH WAS PERHAPS YOUR

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16 1 FIRST PIECE ON TRYING TO DETECT THE SICKLE CELL GENOME, DID YOU
2 PUBLISH OTHER ARTICLES ON YOUR EFFORTS TO IMPROVE THAT METHOD?
3 A. WELL, WE FIRST PUBLISHED THIS IN 1981, ACTUALLY, WHERE WE
4 DETECTED THE SICKLE CELL GENE IN 1981. I'VE PUBLISHED OTHER
5 ARTICLES SINCE.

6 Q. SO IN 1981, YOU PUBLISHED AN ARTICLE AND THEN, IN 1983, YOU
7 AND DR. CONNER AND SOME OTHERS PUBLISHED ONE?

8 A. YES.

9 (PAUSE IN PROCEEDINGS)

10 Q. (BY MR. PASAHOW) LET ME SHOW YOU WHAT WE'VE MARKED AS
11 EXHIBIT B-148.

12 A. (WITNESS EXAMINES DOCUMENT.)

13 Q. YOU'RE A CO-AUTHOR OF THAT ARTICLE?

14 A. I AM.

15 Q. WHAT'S THE SUBJECT OF THAT ARTICLE?

16 A. THIS WAS A -- AN ARTICLE DESIGNED TO IMPROVE THE SIGNAL
17 OBTAINED FROM THE PROBE.

18 IT'S ENTITLED: "ALLELE-SPECIFIC HYBRIDIZATION
19 USING OLIGONUCLEOTIDE PROBES OF VERY HIGH SPECIFIC
20 ACTIVITY: DISCRIMINATION OF THE HUMAN BETA A AND BETA
21 S GLOBIN GENES" -- BETA S IS THE SICKLE CELL GENE --
22 BY ANNA STUDENICKI AND MYSELF.

23 Q. AND SO WHAT YOU WERE TRYING TO DO WAS MAKE THE PROBES THAT
24 YOU USED EXTRA RADIOACTIVE, IF YOU WILL?

25 A. YES.

WALLACE-CROSS/PASAHOW

16 1 Q. AND YOU HOPED, BY MAKING THEM MORE RADIOACTIVE, YOU'D MAKE
2 YOUR TESTS MORE SENSITIVE?

3 A. THAT'S CORRECT.

4 Q. BY THAT METHOD, WERE YOU ABLE TO MAKE YOUR TESTS AS
5 SENSITIVE AS PCR WOULD HAVE MADE IT?

6 A. AS PCR WOULD HAVE MADE IT WHEN? TODAY? NO. PCR'S MUCH
7 MORE SENSITIVE TO DATE THAN WE WERE ABLE TO MAKE IT.

8 Q. HOW ABOUT IN 1985? WAS PCR MORE SENSITIVE IN 1985 AS A --

9 A. YES. AS I SAID, I THINK I -- IN 1985, THE DETECTION BY PCR
10 WAS -- WAS MORE SENSITIVE THAN THIS.

11 (PAUSE IN PROCEEDINGS)

12 Q. (BY MR. PASAHOW) SO THIS ARTICLE WITH THE HIGHLY
13 RADIOACTIVE PROBES WAS PUBLISHED IN 1985, YOU INDICATED?

14 A. I DON'T . . . BELIEVE SO. I THINK IT WAS 1984.

15 Q. 1984. THANK YOU.

16 DID YOU THEN TRY OTHER DETECTION METHODS TO TRY TO
17 DETECT THE SICKLE CELL GENE?

18 (PAUSE IN PROCEEDINGS)

19 THE WITNESS: I'M NOT SURE WHICH OTHER METHODS YOU'RE
20 TALKING ABOUT.

21 WE MAINLY RELIED ON RADIOACTIVE DETECTION. WE HAD
22 PUBLISHED SOME WORK ON BIOTIN DETECTION, BUT I DON'T RECALL IF
23 WE HAD USED BIOTIN DETECTION FOR SICKLE CELL.

24 Q. (BY MR. PASAHOW) LET ME SHOW YOU WHAT WE'VE MARKED AS
25 EXHIBIT B-147. IT MAY HELP YOU ANSWER THAT.

WALLACE-CROSS/PASAHOW

16 1 A. (WITNESS EXAMINES DOCUMENT.)

2 Q. NOW, B-147 IS ANOTHER ARTICLE THAT YOU CO-AUTHORED?

3 A. YES, IT IS.

4 Q. AND THIS WAS ABOUT THE EFFORT YOU MADE TO TRY TO USE A
5 DIFFERENT KIND OF PROBE; IS THAT RIGHT?

6 A. YES. IT WAS A PROBE -- I'M -- WELL, IT COVERED MORE THAN
7 THAT, BUT IT INCLUDED STUDIES ON MAKING A DIFFERENT KIND OF
8 PROBE, THAT'S CORRECT, A SO-CALLED BIOTIN-LABELED PROBE.

9 Q. AND THAT, AGAIN, WAS A PROBE TO TRY TO DETECT THE SICKLE
10 CELL GENE.

11 A. NO, I DON'T THINK SO. IT WAS DESIGNED -- LET ME JUST SEE.

12 (PAUSE IN PROCEEDINGS)

17 13 THE WITNESS: THIS PROBE IS DESIGNED TO DETECT A MOUSE
14 GENE.

15 (PAUSE IN PROCEEDINGS)

16 Q. (BY MR. PASAHOW) COULD THAT KIND OF A PROBE BE USED IN A
17 SICKLE CELL TEST?

18 A. WELL, WE FOUND THAT THESE PROBES WERE NOT AS SENSITIVE AS
19 RADIOACTIVE PROBES.

20 (PAUSE IN PROCEEDINGS)

21 THE WITNESS: SO WE DON'T USE THEM FOR THAT KIND OF
22 TEST.

23 Q. (BY MR. PASAHOW) WHAT YOU FOUND IS THAT THEY -- THEY
24 WEREN'T SENSITIVE ENOUGH TO BE USED TO TRY TO DETECT A HUMAN
25 GENOMIC DISEASE, LIKE SICKLE CELL?

WALLACE-CROSS/PASAHOW

17 1 A. THIS PARTICULAR KIND OF PROBE WAS NOT BEING USED FOR THAT,
2 THAT'S RIGHT.

3 Q. BUT YOU THOUGHT THAT IF YOU CAN IMPROVE THE SENSITIVITY BY
4 50 OR A HUNDRED-FOLD, IT COULD BE USED FOR THAT PURPOSE; IS THAT
5 RIGHT?

6 A. IF THE PROBE SENSITIVITY COULD HAVE BEEN IMPROVED, IT COULD
7 HAVE BEEN USED, YES. ABOUT A 50- TO A HUNDRED-FOLD LESS
8 SENSITIVE, I GUESS, IS WHAT THAT SENTENCE MEANS, THAN
9 RADIOACTIVE PROBES.

10 Q. NOW, IF YOU TOOK YOUR SAMPLE WITH THE SICKLE CELL GENE IN
11 IT --

12 A. UH-HUH.

13 Q. -- AND YOU FIRST AMPLIFIED IT WITH PCR, COULD YOU HAVE USED
14 THESE NON-RADIOACTIVE PROBES?

15 A. YES, YOU COULD HAVE.

16 (PAUSE IN PROCEEDINGS)

17 Q. (BY MR. PASAHOW) NOW, IN DISCUSSING DOUBLE-STRANDED
18 SEQUENCING WITH MR. FIGG, YOU SUGGESTED THAT SOME OF THOSE
19 ARTICLES WOULD HAVE TAUGHT AN ORDINARILY-SKILLED SCIENTIST IN
20 1984 HOW TO USE A PRIMER EXTENSION REACTION WITH DOUBLE-STRANDED
21 DNA?

22 A. THAT'S CORRECT.

23 Q. LET ME ASK THIS: ARE THE CONDITIONS THAT YOU'D USE FOR ONE
24 OF THESE DOUBLE-STRANDED SEQUENCING REACTIONS CONDITIONS THAT
25 WOULD BE USEFUL IN A PCR REACTION?

WALLACE-CROSS/PASAHOW

17 1 A. PROBABLY AMONGST THE CONDITIONS, YES.

2 Q. HAVE YOU EVER INVESTIGATED THAT?

3 A. I DON'T KNOW IF WE . . . HAVE EVER DONE THAT EXPERIMENT, NO.

4 Q. YOU DO RECALL, SIR, THAT YOU HAVE NEVER INVESTIGATED THE
5 QUESTION WHETHER THE CONDITIONS FOR PCR CAN BE FOUND BY GOING TO
6 THIS LITERATURE ON DOUBLE-STRANDED SEQUENCING AND TRYING TO
7 APPLY THEM.

8 A. WELL, I DON'T KNOW WHAT CONDITIONS YOU MEAN. THE -- THERE'S
9 LOTS OF CONDITIONS FOR DOING PCR.

10 Q. UH-HUH. WHERE WOULD I GET THOSE CONDITIONS IN 1984 IF I
11 WERE TRYING TO DO A PCR REACTION?

12 A. I THINK YOU WOULD INVESTIGATE BY ROUTINE INVESTIGATION. IF
13 THE CONDITIONS OF A SEQUENCING REACTION DIDN'T WORK, THEN YOU'D
14 USE ROUTINE INVESTIGATION.

15 Q. WHAT DOES "ROUTINE INVESTIGATION" MEAN AS YOU USE IT?

16 A. WELL, YOU WOULD ASK YOURSELF WHAT'S IMPORTANT. I MEAN, FOR
17 EXAMPLE, IF YOU TURN TO THE PATENT, THEY USE WIDELY DIFFERENT
18 CONDITIONS. ARE THEY AMONGST ALL OF THE CONDITIONS OR NOT?

19 YOU ASK YOURSELF THOSE QUESTIONS. IN THE PRIOR ART,
20 WHAT HAS WORKED? WE KNOW THAT PRIMER EXTENSIONS WORK UNDER THE
21 CONDITIONS OF A PARTICULAR REACTION, FOR EXAMPLE, SEQUENCING
22 REACTION.

23 SO THAT'S YOUR STARTING POINT. YOU ASK YOURSELF: WHAT
24 WILL -- WHAT ARE THE RESULTS OF THE REACTION? AND IF THEY'RE
25 EITHER GOOD OR BAD, THEN YOU CHANGE THINGS ACCORDINGLY.

WALLACE-CROSS/PASAHOW

17 1 Q. WELL, SUPPOSE I DO THE REACTION AND I DON'T GET ANY RESULT.

2 A. BUT YOU WOULD. THE SEQUENCING WORKS.

3 Q. I BEG YOUR PARDON?

4 A. YOU WOULD, BECAUSE YOU KNOW THAT DOUBLE -- PRIMING OF A
5 DOUBLE-STRANDED DNA GIVES A PRODUCT. I MEAN, THAT'S WHERE
6 YOU'RE STARTING FROM, FROM A POSITIVE RESULT.

7 Q. WELL, BUT -- BUT -- THERE'S A SET OF CONDITIONS THAT YOU USE
8 IN SEQUENCING TO GET PRIMERS TO GO JUST A LIMITED AMOUNT DOWN --
9 DOWN THE CHAIN. THEY DON'T GO TO THE END.

10 A. WELL, THOUSANDS OF NUCLEOTIDES PROBABLY. HUNDREDS AND
11 THOUSANDS OF NUCLEOTIDES, BUT . . .

12 Q. THEY DON'T ALL GO HUNDREDS OR THOUSANDS.

13 A. A LOT OF THEM DO, ACTUALLY, YEAH.

14 Q. WELL, ISN'T THE WHOLE POINT OF DOUBLE-STRANDED SEQUENCING TO
15 MAKE THEM STOP ALONG THE WAY?

16 A. WELL, IT'S, OF COURSE, THROUGH YOUR UNDERSTANDING OF THE DNA
17 SEQUENCING PROCESS THAT YOU CAUSE IT TO BE INTERRUPTED DURING
18 ITS TRAVEL DOWN THE MOLECULE, THAT'S TRUE. IT STOPS --
19 DEPENDING ON HOW YOU SET IT UP -- EVERY HUNDREDTH OR EVERY
20 200TH, DEPENDING ON THE -- ON AVERAGE, DEPENDING ON THE
21 EXPERIMENT.

22 Q. SO IN A DOUBLE-STRANDED SEQUENCING METHOD, YOU SET IT UP SO
23 THAT IT STOPS AS IT GOES DOWN THE MOLECULE. IT DOESN'T GO --

24 A. SOME OF THE -- SOME OF THE PRIMER EXTENSIONS STOP AS IT GOES
25 DOWN THE MOLECULE, THAT'S TRUE.

WALLACE-CROSS/PASAHOW

17 1 Q. NOW, YOU WANT IT TO STOP AT JUST THE RIGHT PLACE; DON'T YOU?

2 A. OH, YOU STOP THEM WITH ANALOGS TO THE BUILDING BLOCKS, AS I
3 THINK DR. KORNBERG TALKED ABOUT.

4 Q. BUT YOU -- YOU DON'T WANT THEM TO JUST STOP PART WAY DOWN
5 THE CHAIN AT ANY RANDOM SPOT. YOU WANT THEM TO GO ALL THE WAY
6 TO THE POINT WHERE IT WOULD INCORPORATE THIS BLOCKING DIDEOXY
7 THING?

18 8 A. YEAH. THAT'S WHY SEQUENCING WORKS. DNA POLYMERASE DOESN'T
9 JUST STOP.

10 Q. WELL, ARE THERE REQUIREMENTS FOR MAKING SURE THAT THIS
11 SEQUENCING REACTION TERMINATES AT A DIDEOXY RATHER THAN JUST
12 STOP AT ANY PLACE, ARE THOSE REQUIREMENTS DIFFERENT FROM THE
13 REQUIREMENTS FOR INSURING THAT YOU GET COMPLETE EXTENSION IN A
14 PCR REACTION?

15 A. PROBABLY AMONGST THE CONDITIONS. WE'VE DONE PRIMER
16 EXTENSIONS THAT DO GO ALL THE WAY TO THE END ON PURPOSE AND
17 THOSE ONES USE VERY SIMILAR CONDITIONS.

18 Q. YOU DO RECALL, SIR, THAT YOUR DEPOSITION WAS TAKEN BY ME IN
19 THIS CASE.

20 A. YES, I DO.

21 Q. AND YOU RECALL, OF COURSE, THAT BEFORE THAT DEPOSITION, YOU
22 TOLD US, JUST AS BEFORE YOU TESTIFIED, THAT YOU WERE GOING TO
23 TELL THE TRUTH AS WELL AS YOU COULD?

24 A. I DID.

25 Q. DOCTOR, ON PAGE 181 OF THAT DEPOSITION, THE REPORTER

WALLACE-CROSS/PASAHOW

18 1 RECORDED THIS TESTIMONY, BETWEEN LINES 15 AND 21: I ASKED:

2 "ARE THERE REQUIREMENTS FOR MAKING SURE THAT
3 IT DOES TERMINATE AT A DIDEOXY RATHER THAN JUST STOP"
4 AT ANY DIFFERENT PLACE -- "STOP ANY DIFFERENT THAN THE
5 REQUIREMENTS FOR INSURING COMPLETE EXTENSION TO PCR?"

6 AND AT THAT TIME YOU TOLD ME:

7 "I DON'T KNOW. I HAVEN'T INVESTIGATED,
8 EITHER, UNDER EACH OTHER'S CONDITIONS, TO KNOW THAT TO
9 BE IN ANY WAY."

10 A. THAT'S WHAT I'VE ALREADY TESTIFIED TO. I DON'T KNOW IF THE
11 CONDITIONS OF A . . . A SEQUENCING REACTION ARE OPTIMAL FOR PCR.
12 I HAVEN'T INVESTIGATED THAT.

13 Q. WELL --

14 A. BUT YOU'RE ASKING ME WHETHER THE CONDITIONS THAT CAUSE IT TO
15 TERMINATE WILL GIVE A PCR REACTION.

16 THE CONDITIONS THAT CAUSE IT TO TERMINATE INCLUDE, FOR
17 EXAMPLE, DIDEOXY NUCLEOTIDES, THESE ANALOGS THAT DR. KORNBERG
18 TALKED ABOUT. YOU DON'T PUT THESE INTO A PCR REACTION, SO
19 THEY'RE DIFFERENT CONDITIONS.

20 Q. LET ME TRY THIS A DIFFERENT WAY:

21 WERE PEOPLE OF ORDINARY SKILL IN THE ART DOING THEIR
22 SEQUENCING WITH THESE DOUBLE-STRANDED SEQUENCING REACTIONS YOU
23 DESCRIBED TO US?

24 A. I DON'T KNOW HOW WIDELY SPREAD -- HOW WIDELY SPREAD IT WAS.
25 WE PUBLISHED IT; OTHER PEOPLE PUBLISHED USING THOSE PROCEDURES.

WALLACE-CROSS/PASAHOW

18 1 Q. IN 1984, IS THAT WHAT PEOPLE IN YOUR LABORATORY USED?

2 A. WE USED IT, YES.

3 Q. IN 1984?

4 A. WE HAVE USED IT. WE'VE ALSO USED SINGLE-STRANDED
5 SEQUENCING, DEPENDENT ON THE -- WE ALSO USED CHEMICAL
6 SEQUENCING. THERE ARE MANY WAYS OF DOING SEQUENCING. WE USED A
7 COMBINATION. WE PUBLISHED THE --

8 OH, IN 1984. EXCUSE ME.

9 Q. YES, SIR.

10 A. I DON'T KNOW. I DON'T REMEMBER IF WE USED IT IN 1984. WE
11 PUBLISHED A PAPER IN 1981, TWO PAPERS USING IT IN 1981.

12 Q. UH-HUH. IN 1984, YOUR LABORATORY WAS LARGELY USING A
13 DIFFERENT METHOD CALLED THE MAXIM GILBERT (PHONETIC) METHOD?

14 A. FOR SOME SEQUENCING PROJECTS, WE USED MAXIM GILBERT. IN
15 1984? PROBABLY MOST OF THE TIME.

16 Q. UH-HUH. AND THAT METHOD DOESN'T INVOLVE TRYING TO SEQUENCE
17 USING DOUBLE-STRANDED DNA AND RUNNING A PRIMER THROUGH IT.

18 A. IT USES DOUBLE-STRANDED -- IT USES DOUBLE-STRANDED DNA.

19 Q. IT DOESN'T USE A PRIMER EXTENSION REACTION?

20 A. NO. IT'S COMPLETELY DIFFERENT. IT USES CHEMICAL REACTIONS.

21 Q. NOW, YOU RECALL THIS ARTICLE FROM DR. HONG THAT YOU AND MR.
22 FIGG DISCUSSED, THE ONE THAT HAD THIS CIRCULAR PIECE AND THE
23 PRIMERS GOING BOTH WAYS?

24 A. UH-HUH.

25

(PAUSE IN PROCEEDINGS)

WALLACE-CROSS/PASAHOW

18 1 Q. (BY MR. PASAHOW) DO YOU STILL HAVE THAT PAPER UP THERE?

2 IT'S A-109.

3 A. (WITNESS SEARCHES THROUGH DOCUMENTS.)

4 YES. A-109?

5 Q. YES.

6 A. THAT'S NOT A-109.

7 I THINK THAT WAS -- WE MIXED THAT UP YESTERDAY.

8 A-109'S THE OTHER HONG.

9 Q. OH, I'M SORRY. OKAY.

10 (PAUSE IN PROCEEDINGS)

11 Q. (BY MR. PASAHOW) IS THAT THE 1981 OR THE 1982 HONG PAPER?

12 A. '82.

13 (PAUSE IN PROCEEDINGS)

14 Q. (BY MR. PASAHOW) DO YOU HAVE A COPY?

15 A. I HAVE A COPY OF THAT ONE. I DON'T HAVE A COPY -- I DIDN'T
16 FIND A COPY OF THE OTHER ONE.

17 Q. YOU DO HAVE A-109?

18 A. 109, YEAH.

19 Q. NOW, DR. HONG APPARENTLY TRIED OUT YOUR METHOD AS WELL IN
20 THE COURSE OF DOING HIS WORK; IS THAT RIGHT?

21 A. HE REFERS TO IT, YES.

22 Q. AND WHAT HE SAYS IS, IS THAT IT DIDN'T WORK VERY WELL; ISN'T
23 THAT RIGHT?

24 A. NO. I DON'T -- WOULDN'T INTERPRET THAT. HE SAYS THAT:

25 "RECENTLY, THE M13 REVERSE-SEQUENCING

WALLACE-CROSS/PASAHOW

18 1 METHOD" -- WHICH IS THE OTHER HONG PAPER -- "AND THE
2 SEQUENCING OF PBR322 DNA" -- AND I GUESS ONE OF THOSE
3 IS MY TWO PAPERS ON THE SUBJECT -- "HAVE SHOWN THAT IT
4 IS POSSIBLE TO SEQUENCE . . ."

5 THERE'S A WORD MISSING HERE.

6 (PAUSE IN PROCEEDINGS)

7 THE WITNESS: ARE YOU -- IS IT THE SAME THING THAT'S ON
8 THE POSTER?

9 Q. (BY MR. PASAHOW) NO. THIS IS A DIFFERENT PAGE, SIR.

10 A. WHAT ARE YOU . . .

11 ". . . DOUBLE-STRANDED DNA MOLECULES." THAT'S WHAT HE
12 SAID.

13 "HOWEVER, SUCH PROCEDURES HAVE" --

14 SOMETHING -- "BEEN SUCCESSFUL -- HAVE NOT BEEN

15 SUCCESSFUL WITH LARGE DOUBLE-STRANDED DNA MOLECULES."

16 Q. WELL, YOUR PAPER IS WHAT'S REFERRED TO AS NUMBER SIX IN THIS
17 ARTICLE; IS THAT RIGHT?

18 A. (WITNESS EXAMINES DOCUMENT.)

19 YES, NUMBER SIX, AND THEN WE DID IT AGAIN IN NUMBER
20 SEVEN.

21 Q. AND HE'S DISCUSSING YOUR PAPER AT THE END OF THE ARTICLE,
22 AND THERE HE SAYS:

23 "INITIAL EXPERIMENTS USING METHODS PREVIOUSLY
24 DESCRIBED GAVE VERY POOR RESULTS. RATHER SPECIFIC
25 CONDITIONS ARE REQUIRED TO GIVE SATISFACTORY RESULTS.

WALLACE-CROSS/PASAHOW

19 1 PRESUMABLY, IT IS NECESSARY FOR TWO LAMBDA STRANDS TO
2 REMAIN DENATURED WHILE THE PRIMER ANNEALS TO THE
3 TEMPLATE. ANNEALING AT ROOM TEMPERATURE PRODUCES VERY
4 WEAK SEQUENCING PATTERNS, WHICH ARE MASKED BY THE
5 PRESENCE OF ARTIFACT BANDS."

6 DO YOU SEE THAT PART OF THE ARTICLE?

7 A. YES.

8 Q. YOU AGREE, EVEN IN DR. HONG'S HANDS, YOUR METHOD DIDN'T WORK
9 VERY WELL?

10 A. HE'S NOT TALKING ABOUT MY METHOD.

11 Q. NUMBER SIX?

12 A. HE'S USING -- HE'S GIVING REFERENCE TO THOSE PAPERS YOU'RE
13 USING, DOUBLE-STRANDED SEQUENCING ON LAMBDA DNA'S. THAT WAS MY
14 WORK.

15 Q. UH-HUH.

16 A. THIS IS ON LAMBDA DNA IS WHAT I UNDERSTOOD. IT'S AN
17 APPROXIMATELY 10 TIMES LARGER PIECE OF DNA.

18 SO HE FOUND THAT . . . THAT'S THE WAY I READ IT. I
19 UNDERSTOOD WHAT YOU JUST SAID, IS THAT SPECIFIC CONDITIONS WERE
20 REQUIRED FOR THIS LAMBDA DNA TEMPLATE.

21 Q. WELL, HE -- IN THE MIDDLE OF THAT, HE SPECIFICALLY REFERS TO
22 YOUR ARTICLE, TO NUMBER SIX.

23 HE SAYS: "ANNEALING AT ROOM TEMPERATURE" --
24 REFERRING TO FOUR SIX AND SEVEN, SIX BEING YOUR
25 ARTICLE -- "PRODUCES VERY WEAK SEQUENCING PATTERNS,

WALLACE-CROSS/PASAHOW

19

1 WHICH ARE" --

2 A. ON LAMBDA DNA.

3 Q. -- "MASKED BY THE PRESENCE OF ARTIFACT BANDS."

4 A. PRESUMABLY THAT'S ON LAMBDA DNA.

5 Q. I SEE.

6 A. ON LAMBDA DNA. IT'S LIKE PCR NOT WORKING. MAYBE THIS IS AN
7 EXAMPLE OF THAT.8 Q. AND SO AT LEAST IN HIS -- WITH HIS DNA, YOUR METHOD DIDN'T
9 WORK VERY WELL.

10 A. IT WORKED BUT NOT VERY WELL FOR HIM.

11 Q. IT GAVE POOR RESULTS.

12 A. THAT'S WHAT HE SAID.

13 Q. NOW, OTHERS HAVE FOUND THAT THE HONG METHOD DIDN'T WORK VERY
14 WELL; ISN'T THAT RIGHT?

15 A. I DON'T KNOW.

16 (PAUSE IN PROCEEDINGS)

17 Q. (BY MR. PASAHOW) LET ME SHOW YOU EXHIBIT A-112. THAT'S A
18 PAPER BY A GROUP OF DU PONT SCIENTISTS?

19 A. (WITNESS EXAMINES DOCUMENT.)

20 IT WOULD APPEAR SO.

21 Q. NOW, THE HONG METHOD, YOU'VE TOLD US, WAS FOR USE WITH
22 LAMBDA DNA; IS THAT RIGHT?

23 A. AND THE M13 REVERSE PRIMER METHOD.

24 Q. NOW, IF YOU'LL TURN TO THE END OF THIS ARTICLE, THEY DISCUSS
25 USING THE HONG METHOD FOR SEQUENCING LAMBDA DNA.

WALLACE-CROSS/PASAHOW

19 1 MR. FIGG: YOUR HONOR, MR. PASAHOW HASN'T ESTABLISHED
2 WHETHER DR. WALLACE HAS EVER READ THIS PAPER BEFORE.

3 THE COURT: WELL, I THINK IF HE HAS SUFFICIENT TIME TO
4 REVIEW IT NOW, HE CAN ANSWER THAT QUESTION.

5 CAN YOU DO THAT?

6 THE WITNESS: IF I HAVE TIME TO READ IT? I'LL JUST
7 READ THROUGH IT.

8 MR. PASAHOW: YOUR HONOR, IT'S A DOCUMENT THAT DU PONT
9 DESIGNATED AND THAT WAS PUT IN EVIDENCE AS PART OF THE ART IT
10 WANTED TO REFER TO.

11 THE COURT: UH-HUH.

12 MR. FIGG: I'M NOT OBJECTING TO --

13 THE COURT: WELL --

14 MR. FIGG: -- REFERENCE TO THE ARTICLE, BUT IF DR.
15 WALLACE IS GOING TO BE QUESTIONED ABOUT IT, I DON'T -- I THINK
16 WE NEED TO KNOW WHETHER HE KNOWS ANYTHING ABOUT THE ARTICLE.

17 THE COURT: EVEN IF HE'D SEEN IT BEFORE, HE MIGHT NEED
18 TO REFRESH HIS RECOLLECTION. I DOUBT THAT HE HAS EVERY
19 PARAGRAPH COMMITTED TO MEMORY, OR MAYBE HE DOES. I DON'T KNOW.

20 THE WITNESS: AFRAID NOT, YOUR HONOR.

21 (PAUSE IN PROCEEDINGS)

22 THE WITNESS: OH, PERHAPS I NEED TO KNOW WHAT YOUR
23 QUESTION'S GOING TO BE, SO . . .

24 Q. (BY MR. PASAHOW) I WAS GOING TO REFER YOU TO THE PORTION ON
25 PAGE 92 WHERE THEY'RE TALKING ABOUT SEQUENCING LAMBDA DNA.

WALLACE-CROSS/PASAHOW

19 1 THAT'S WHAT THAT GREEK LETTER THERE IS; IS THAT CORRECT?

2 A. RIGHT. LAMBDA DNA IS THE LARGE VIRAL -- THE DNA FROM THE
3 VIRUS CALLED BACTERIOPHAGE LAMBDA, WHICH IS REFERRED TO ON THAT
4 CHART OVER THERE.

5 Q. AND HERE THEY SAY:

6 "A METHOD FOR SEQUENCING LARGE

7 DOUBLE-STRANDED DNA MOLECULES WAS DEVELOPED BY HONG."

8 A. YES.

9 Q. AND THEY HAVE THE REFERENCE FOUR, AND THAT'S A REFERENCE TO
10 THE ARTICLE YOU DISCUSSED WITH MR. FIGG; IS THAT RIGHT?

11 A. YES.

12 Q. AND THEY SAY:

13 "HOWEVER, HONG'S PROTOCOL DOES NOT WORK WELL

14 ON LAMBDA DNA."

15 IS THAT RIGHT?

16 A. IT GOES ON, YEAH.

17 IT SAYS: "IN OUR INITIAL ATTEMPT TO SEQUENCE FROM

18 LAMBDA, WE TRIED USING THE PLASMID DNA SEQUENCING

19 PROCEDURE WITH KLENOW DNA POLYMERASE 1, BUT ONLY THE

20 FIRST 100 BASES WERE READABLE." SO . . . YEAH.

21 Q. SO, AT LEAST FOR THESE DU PONT SCIENTISTS, THE HONG
22 DOUBLE-STRANDED METHOD DIDN'T WORK VERY WELL.

23 A. WELL, YOU HAVE TO ASK YOURSELF, WORK WITH RESPECT TO WHAT?
24 YOU'RE TRYING TO SAY THAT PRIMER EXTENSION DOESN'T WORK OR THAT
25 SEQUENCING ISN'T SPECIFIC.

WALLACE-CROSS/PASAHOW

20 1 AND I THINK WHAT THEY'RE SAYING IS THAT THEY WEREN'T
2 ABLE TO DEDUCE A SUBSTANTIAL AMOUNT OF SEQUENCE INFORMATION.
3 THAT DOESN'T IMPLY THAT PRIMER EXTENSION DIDN'T WORK. IN FACT,
4 IT DID. IT DIDN'T WORK WELL.

5 Q. LET ME SHOW YOU WHAT WE MARKED AS EXHIBIT B-152. YOU'VE
6 SEEN THAT ARTICLE BEFORE?

7 A. YES, I HAVE.

8 Q. AND THIS WAS AN ARTICLE PUBLISHED BY TWO SCIENTISTS AT
9 GENENTECH; IS THAT CORRECT?

10 A. THEY WERE AT GENENTECH AT THE TIME, YES.

11 Q. AND THEY, TOO, DESCRIBED A METHOD OF SEQUENCING
12 DOUBLE-STRANDED DNA; IS THAT RIGHT?

13 A. THAT'S CORRECT.

14 Q. NOW, IN THE METHOD THEY USED, THEY WOULD TREAT THE
15 DOUBLE-STRANDED DNA IN A SPECIAL WAY SO THAT, AFTER YOU HEATED
16 IT UP ONCE, IT COULDN'T COME BACK TOGETHER; IS THAT CORRECT?

17 A. WELL, THAT'S THE . . . HYPOTHESIS.

18 Q. THAT AT LEAST IS WHAT THEY WERE TRYING TO DO.

19 A. YEAH. YEAH, RIGHT.

20 Q. SO IT WOULD BE IRREVERSIBLY TORN APART AND THE TWO STRANDS
21 COULD NEVER COME BACK TOGETHER.

22 A. AGAIN, THAT'S THE HYPOTHESIS THEY'RE BASING THE METHOD ON.

23 Q. NOW, THEY, TOO, DESCRIBE OTHER METHODS THAT HAD BEEN TRIED
24 EARLIER; IS THAT RIGHT? ON THE SECOND COLUMN ON PAGE 166.

25 A. UH-HUH.

WALLACE-CROSS/PASAHOW
(PAUSE IN PROCEEDINGS)

20

1

2

THE WITNESS: THAT'S CORRECT.

3

Q. (BY MR. PASAHOW) AND AMONG OTHERS, THEY REFER TO YOUR
ARTICLE?

4

5

A. WELL, THEY SAY:

6

"A MAJOR DRAWBACK OF THIS METHOD IS THAT DNA
OF LOW COMPLEXITY RENATURES RAPIDLY, LEAVING NO
SINGLE-STRANDED TEMPLATE AVAILABLE."

7

8

9

10

11

12

13

14

SO THAT THEY JUSTIFY DOING WHAT THEY WERE DOING ON THE
BASIS OF THE FACT THAT THEY ASSUME THAT THIS METHOD, WHICH
THEY . . . WHICH THEY USE, WHICH IS TO USE ALKALI TO THE
DENATURATION STEP INSTEAD OF . . . INSTEAD OF HEATING, AND THEY
USED CO-VALENTLY-CLOSED CIRCULAR DNA. PLASMA THAT IS STILL IN
THE CIRCULAR FORM.

15

16

IF THEY MAKE THOSE TWO THINGS, THEN THEY FIND THAT
RESULTS ARE BETTER.

17

18

19

BUT IF YOU TURN TO FIGURE 1, YOU CAN SEE THAT,
NEVERTHELESS, THE METHOD WE DESCRIBED WORKED QUITE WELL,
ACTUALLY.

20

21

22

Q. WELL, WHAT THEY SAY ABOUT IT IS THAT THE SUCCESS OF USING
DOUBLE-STRANDED DNA FOR SEQUENCING DEPENDS UPON THE ABILITY TO
KEEP THE TWO STRANDS FROM COMING BACK TOGETHER.

23

A. AND THEN GO ON TO SHOW THAT THAT'S NOT A PROBLEM.

24

25

Q. AND THEY THEN SAY THAT THE MAJOR DRAWBACK OF YOUR METHOD IS
THAT THE DNA IS OF LOW COMPLEXITY AND IT COMES BACK TOGETHER

20 1 RAPIDLY.

2 THAT WAS THEIR VIEW, WHETHER IT'S YOUR VIEW OR NOT; IS
3 THAT RIGHT?

4 A. NO. THEIR VIEW -- THAT WASN'T THEIR VIEW. THEIR VIEW OF
5 DNA OF LOW COMPLEXITY DIDN'T COME BACK TOGETHER, AND RENATURED
6 RAPIDLY, AND THAT THAT COULD BE A DRAWBACK OF THE METHOD. WE
7 SHOWED THAT IT WASN'T A PROBLEM AND THEY SHOWED IT WASN'T A
8 PROBLEM.

9 Q. THAT IT WAS NOT A PROBLEM.

10 A. OTHERWISE, SEQUENCING WOULDN'T WORK; WOULD IT?

11 Q. NOW, YOU'RE FAMILIAR WITH A SERIES OF BOOKS THAT GOES BY THE
12 NAME OF MOLECULAR CLONING, OR, THE SHORT FORM, THE CLONING
13 MANUAL; IS THAT RIGHT?

14 A. YES.

15 Q. AND THIS IS A RATHER FAMOUS SERIES OF BOOK -- BOOKS THAT
16 HAVE BEEN PUT OUT FROM TIME TO TIME?

17 A. WELL, I THINK IT'S ONLY BEEN PUT OUT TWICE, BUT -- TO MY
18 KNOWLEDGE. THIS IS THE SECOND EDITION.

19 Q. AND THAT'S FROM A 1989 VERSION?

20 A. THIS IS VOLUME 2 FROM 1989.

21 Q. NOW, IN THERE, THEY DISCUSS THESE VARIOUS EFFORTS TO -- TO
22 DO DOUBLE-STRANDED SEQUENCING; IS THAT -- IS THAT CORRECT?

23 A. I DON'T KNOW.

24 Q. WHY DON'T YOU LOOK AT PAGE 13.7, PLEASE.

25 A. (WITNESS EXAMINES PAGE FROM BOOK.) YES.

WALLACE-CROSS/PASAHOW

20 1 Q. AND, OF COURSE, THEY RECOMMENDED THAT SEQUENCING BE DONE ON
2 SINGLE-STRANDED DNA; IS THAT RIGHT?

3 A. WELL, I THINK THEIR RECOMMENDATION HAS TO DO WITH THE
4 ABILITY TO INTERPRET SEQUENCE AS OPPOSED TO THE PRIMER EXTENSION
5 REACTION. I THINK YOU HAVE TO DISCRIMINATE BETWEEN THOSE TWO --
6 TWO THINGS.

7 "THE BEST RESULTS ARE OBTAINED FROM
8 SINGLE-STRANDED DNA TEMPLATES."

9 Q. NOW, THIS BOOK --

10 A. IS WHAT IT SAYS.

11 Q. I'M SORRY?

12 A. THAT'S WHAT IT SAYS. I'M SORRY. THAT WAS NOT MY OWN. I'M
13 READING.

14 Q. THIS BOOK IS -- IN THE SERIES, IT'S VERY WELL RESPECTED
15 AMONG THOSE WHO ARE IN THE FIELD OF BIOTECHNOLOGY; ISN'T THAT
16 RIGHT?

17 A. I THINK SO. THAT WOULD BE A FAIR STATEMENT.

18 Q. AND YOU'D EXPECT THE ORDINARILY-SKILLED PERSON TO RELY ON
19 ITS RECOMMENDATIONS; ISN'T THAT RIGHT?

20 A. YES, I WOULD.

21 Q. AND SO YOU'D EXPECT THE ORDINARILY-SKILLED PERSON THROUGHOUT
22 THIS PERIOD TO HAVE BEEN USING SINGLE-STRANDED SEQUENCING.

23 A. WELL, AS I SAID, I MEAN, I THINK THAT THEY DO REFER TO
24 DOUBLE-STRANDED DNA TEMPLATES THERE, THE CHEN AND SEEBURG
25 REFERENCES REFERENCE, SO THAT YOU WOULD HAVE BEEN AWARE THAT

WALLACE-CROSS/PASAHOW

1 DOUBLE-STRANDED SEQUENCING IS POSSIBLE, SO YOU WOULD HAVE BEEN
2 AWARE THAT PRIMER EXTENSIONS CAN OCCUR ON DOUBLE-STRANDED DNA
3 TEMPLATES.

4 (PAUSE IN PROCEEDINGS)

5 Q. (BY MR. PASAHOW) NOW, IN THE CHEN AND SEEBURG METHOD, THEY
6 GO THROUGH A PROCESS WHERE THEY WOULD MAKE THE DNA UNUSEABLE IN
7 A PCR-TYPE REACTION; ISN'T THAT RIGHT?

8 A. I DON'T KNOW WHAT YOU MEAN BY THAT.

9 Q. AFTER THEY DENATURE THE DOUBLE-STRANDED DNA IN THE CHEN AND
10 SEEBURG METHOD, WILL THE TWO PARTS THAT HAVE COME APART BE
11 USEABLE FOR TEMPLATES IN LATER PARTS OF THE REACTION?

12 A. PROBABLY.

13 Q. AFTER YOU HAD -- HAD DENATURED A SUPER-COILED PIECE OF DNA,
14 YOU THINK YOU COULD STILL USE IT IN A PCR REACTION?

15 A. WELL, IF YOU'RE ONLY TRYING TO AMPLIFY A SEGMENT OF THAT
16 DENATURED DNA, IT PROBABLY WOULD WORK.

17 Q. AND THEN YOU COULD DENATURE IT AGAIN USING THAT SAME METHOD?

18 A. YOU COULD USE ALKALOID DENATURATION IN EVERY STEP, IF YOU
19 WISHED. IT WOULD BE A BIT CUMBERSOME.

20 Q. HAVE YOU EVER DONE A PCR REACTION THAT WAY?

21 A. NO, BUT IT'S NOT EXCLUDED BY CLAIM 1. IT JUST SAYS
22 "SEPARATE THE STRANDS."

23 Q. HAVE YOU EVER READ A REFERENCE WHERE SOMEONE SUCCESSFULLY
24 DID A PCR REACTION THAT WAY?

25 A. I'M NOT AWARE OF SOMEBODY WHO'S USED ALKALI IN A PCR

WALLACE-CROSS/PASAHOW

1 REACTION.

2 Q. NOW, DR. HONG, THE AUTHOR OF THESE TWO ARTICLES . . .

3 THIS INDICATES THAT HE WAS AT THE MRC LABORATORY AT
4 CAMBRIDGE, ENGLAND.

5 A. THAT'S WHAT IT SAYS, YES.

6 Q. ARE YOU FAMILIAR WITH THAT LABORATORY?

7 A. I -- I KNOW OF THAT LABORATORY, YES.

8 Q. FOR EXAMPLE, IT'S WHERE DR. WATSON AND DR. CRICK DISCOVERED
9 THE MOLECULAR STRUCTURE OF DNA?

10 A. I BELIEVE THAT'S TRUE, YES --

11 Q. NOW --

12 A. -- IN THE EARLY '50'S.

13 Q. WHEN DR. HONG DID THE EXPERIMENT THAT'S DESCRIBED IN HIS
14 1981 ARTICLE, HE HAD PRIMERS FOR BOTH ENDS OF THE SEQUENCE; IS
15 THAT RIGHT?

16 A. THAT'S CORRECT.

17 Q. AND OBVIOUSLY HE HAD POLYMERASE.

18 A. THAT'S CORRECT.

19 Q. AND HE HAD A TEMPLATE.

20 A. THAT'S CORRECT.

21 Q. AND HE HAD THE SEQUENCE INFORMATION.

22 A. THAT'S . . . CORRECT.

23 Q. DID YOU EVER READ ANY REPORTS OUT OF THE MRC LABORATORY IN
24 CAMBRIDGE INDICATING THAT THEY WERE DOING PCR BEFORE THE CETUS
25 SCIENTISTS EXPLAINED HOW?

WALLACE-CROSS/PASAHOW

1 A. IN MY LOOKING AT THIS, I COULD SEE THAT THEY DIDN'T NEED IT.

2 Q. THEY DIDN'T NEED IT?

3 A. WELL, THEY HAD AMPLIFICATION BY CLONING, SO THEY HAD LOTS OF
4 TEMPLATE. I DON'T UNDERSTAND WHY THEY WOULD HAVE USED PCR IN
5 THIS. THIS IS A SEQUENCING STRATEGY, NOT AN AMPLIFICATION
6 STRATEGY.

7 Q. ARE YOU SUGGESTING THAT, IF YOU'VE GOT CLONING, PCR ISN'T OF
8 ANY VALUE?

9 A. PCR CAN BE OF VALUE TO CLONING, BUT CLONING IS A DIFFERENT
10 PROCESS THAN PCR. IT HAS DIFFERENT VIRTUES.

11 Q. I UNDERSTAND THAT. BUT CLONING WAS AVAILABLE IN DECEMBER
12 1985; IS THAT RIGHT?

13 A. IN DECEMBER OF 1985? YES.

14 Q. AND IT'S CERTAINLY BEEN AVAILABLE THROUGHOUT THE TIME SINCE
15 DECEMBER 1985 THROUGH NOW.

16 A. THAT'S TRUE.

17 Q. AND THAT'S THE SAME TIME PERIOD IN WHICH THE -- THE
18 EXPLOSIVE USE OF PCR HAS OCCURRED; ISN'T THAT RIGHT?

19 A. I IMAGINE THERE'S ALSO BEEN AN EXPLOSIVE USE OF CLONING.

20 Q. SO THERE ARE PLENTY OF USES FOR PCR EVEN IF YOU'VE ALREADY
21 GOT CLONING.

22 A. OH, YEAH, OF COURSE. DIAGNOSTIC VALUES AND SO ON.

23 Q. SO THE MERE FACT THAT A LABORATORY KNEW HOW TO CLONE, THAT
24 WOULDN'T STOP THEM FROM DOING PCR IF THEY KNEW HOW.

25 A. IT WOULDN'T STOP THEM IF -- I DON'T KNOW IF THEY DO PCR

WALLACE-CROSS/PASAHOW

1 TODAY.

2 Q. YOU DON'T KNOW IF THE MRC LABORATORY AT CAMBRIDGE HAS EVER
3 DONE PCR?

4 A. NO. I MEAN DR. HONG, FOR EXAMPLE --

5 Q. OH.

6 A. -- OR DR. SANGER.

7 Q. DO YOU KNOW IF THE MRC LABORATORY HAS SCIENTISTS WHO USE
8 PCR?

9 A. I IMAGINE THEY DO.

10 Q. THE MRC LABORATORY, THAT'S THE SAME LABORATORY THAT'S HEADED
11 BY SIR AARON KLUG; IS THAT RIGHT?

12 A. I DON'T KNOW THAT FOR A FACT, BUT . . . SIR AARON KLUG IS
13 THERE, THAT'S CORRECT.

14 (PAUSE IN PROCEEDINGS)

15 Q. (BY MR. PASAHOW) LET'S TURN TO A DIFFERENT SUBJECT.

16 THE COURT: MR. PASAHOW, WOULD THIS BE A GOOD POINT? I
17 THINK THE -- I DON'T KNOW HOW LONG MISS FRANCIS HAS BEEN AT
18 THIS, BUT FOR SOME TIME NOW.

19 LET'S TAKE ABOUT 10 MINUTES. AND LURLINE, TRY TO GET
20 US ALL BACK HERE IN 10 MINUTES, PLEASE --

21 THE CLERK: OKAY.

22 THE COURT: -- SO WE CAN GET STARTED.

23 WE'RE GOING TO FINISH UP WITH DR. WALLACE TODAY,
24 THOUGH; RIGHT?

25 MR. PASAHOW: OH, ABSOLUTELY.

1 THE COURT: OH, ABSOLUTELY. WE ONLY HAVE ONE MORE
2 HOUR; RIGHT?

3 MR. PASAHOW: I HOPE NOT, YOUR HONOR.

4 THE COURT: OKAY. YOU HOPE NOT?

5 MR. PASAHOW: I HOPE I WILL BE DONE IN LESS THAN AN
6 HOUR.

7 THE COURT: YOU WILL FINISH. OKAY. I'M GOING TO HOLD
8 YOU TO THAT.

9 OKAY. YOU MAY STEP DOWN.

10 AND THE JURY IS EXCUSED. PLEASE FOLLOW THE
11 INSTRUCTIONS I'VE GIVEN YOU, AND WE'LL SEE YOU IN ABOUT 10
12 MINUTES.

13 (JURY EXCUSED)

14 (RECESS TAKEN AT 11:54 A.M.)

15
16
17
18
19
20
21
22
23
24
25 (CONTINUED ON NEXT PAGE - NOTHING OMITTED)

WALLACE-CROSS/PASAHOW

1 MR. PASAHOW: SHALL I PROCEED, YOUR HONOR?

2 THE COURT: YOU CERTAINLY MAY.

3 Q. (BY MR. PASAHOW) DR. WALLACE, I PUT IN FRONT OF YOU A
4 PATENT APPLICATION FOR PATENT APPLICATION SERIAL NUMBER 187428
5 WHICH WE'VE MARKED AS EXHIBIT B-188.

6 A. YES.

7 Q. YOU ARE ONE OF THE INVENTORS ON THIS PATENT APPLICATION?

8 A. YES, I AM.

9 Q. WHAT DATE DID YOU SIGN THE OATH ON THIS PATENT APPLICATION?

10 A. IT SAYS 6/27/88.

11 Q. SO JUNE 1988?

12 A. YEAH.

13 Q. NOW, YOU DISCUSSED THE KLEPPE ET AL. REFERENCE WITH MR. FIGG
14 YESTERDAY AND YOU TALKED ABOUT THE WORK THAT WAS IN IT, THE MAIN
15 PART OF THAT PAPER BEFORE YOU GET TO THE LAST PARAGRAPH THAT
16 INVOLVED A SERIES OF SHORT EXTENSION REACTIONS; IS THAT RIGHT?

17 A. WELL, THE MAIN GOAL OF THE PAPER WAS TO INVESTIGATE THE
18 CONDITIONS TO GET PRIMER EXTENSION REACTIONS FOR THIS
19 MULTIPLICATION PROCESS ESTABLISHED.

20 Q. AND IN THAT PAPER DOCTOR KLEPPE AND HIS COLLEAGUES DISCUSSED
21 A SERIES OF EXTENSION REACTIONS THEY HAD DONE?

22 A. YES, THEY DID.

23 Q. AND THEY USED VARIOUS PIECES OF DNA IN THESE EXPERIMENTS
24 WHICH THEY NUMBER ONE THROUGH SIX; IS THAT RIGHT?

25 A. YES, THEY DID.

WALLACE-CROSS/PASAHOW

1 Q. NOW, THE FIRST PIECE OF DNA THAT THEY USED -- YOU MAY WANT
2 TO REFER TO THE ARTICLE WHICH IS EXHIBIT 18 -- THE FIRST PIECE
3 OF DNA THAT THEY USED WAS A SHORT PIECE WHICH WAS A DUPLEX, TWO
4 PIECES OF DNA AND AT ONE END THERE WAS ONE BASE TO FILL IN AND
5 AT THE OTHER END MAYBE EIGHT BASES TO FILL IN?

6 A. TEN BASES TO FILL IN THE OTHER END.

7 Q. NOW, WHEN THESE TWO PIECES OF DNA WERE PUT INTO THEIR
8 REACTION, WERE THEY ALREADY TOGETHER IN A DUPLEX FORM?

9 A. I DON'T REMEMBER HOW THEY . . . ASSEMBLED THE FIRST
10 REACTION. IT WOULD APPEAR SO.

11 Q. SO THEY NEVER HEATED THESE TWO PIECES OF DNA TO GET THEM TO
12 COME APART THEN GO BACK TOGETHER BY COOLING?

13 A. FOR THIS PRIMER EXTENSION REACTION, NO.

14 Q. AS TO ANY OF THE EXPERIMENTS THEY DESCRIBE IN DETAIL, DID
15 THEY GO THROUGH A PROCESS WHERE THEY HEATED AND LET TWO PIECES
16 OF DNA COME BACK TOGETHER?

17 A. THEY LET THE TWO PIECES OF DNA COME TOGETHER FOR THE PRIMER
18 EXTENSION REACTION.

19 Q. WOULD YOU EXPLAIN TO ME PLEASE WHICH EXPERIMENT THEY DID
20 WHERE THEY HAD TWO PIECES OF DNA THAT WERE APART WHICH THEY
21 BROUGHT TOGETHER FOR THIS EXPERIMENT?

22 A. SO, FOR EXAMPLE, IN FIGURE 13 THEY'RE ASSEMBLING PRIMERS AND
23 TEMPLATES, IT WOULD APPEAR. THEY DIDN'T SYNTHESIZE THE DNA
24 TOGETHER, I GUESS IS REALLY WHAT I'M TRYING TO SAY. THEY'RE
25 DIFFERENT PIECES OF DNA, THEY DON'T GET SYNTHESIZED AS A DUPLEX.

WALLACE-CROSS/PASAHOW

1 Q. THEY JUST PUT THE DNA INTO THE TUBE, THEY NEVER HEATED IT
2 THEN LET IT COOL TO COME BACK TOGETHER; IS THAT RIGHT?

3 A. AGAIN, I'D HAVE TO REFER TO THE DETAILS OF THE EXPERIMENT.
4 IF YOU HAVE SEPARATE, SEPARATE SINGLE STRANDS AND YOU BRING THEM
5 TOGETHER THEY CAN COME TOGETHER AND ANNEAL.

6 Q. THAT'S RIGHT. SO THERE'S NO REASON TO HEAT, ISN'T THAT
7 RIGHT?

8 A. UNLESS THEY'RE ALREADY TOGETHER.

9 Q. IN ANY OF THESE EXPERIMENTS DID THEY HEAT TO MAKE THEM COME
10 APART THEN LET THEM COME BACK TOGETHER BY COOLING?

11 A. I DON'T RECALL.

12 Q. NOW, TWO OF THE PIECES OF DNA THEY WERE EXPERIMENTING WITH
13 DNA-V AND DNA-VI THERE THEY DID NOT HAVE SEPARATE PRIMERS AND
14 TEMPLATES; IS THAT RIGHT?

15 A. WELL, DNA-V WAS A MOLECULE WHICH COULD PRIME ON ITSELF,
16 THAT'S TRUE.

17 Q. WHAT DO YOU MEAN BY COULD PRIME ON ITSELF?

18 A. I THINK I EXPLAINED TO THE JURY BEFORE WHAT A HAIR PIN WAS
19 WHERE THE SUM REGION WITHIN THE DNA COULD FIND A COMPLIMENTARY
20 REGION WITHIN ITSELF AND FORM THIS PRIMER TEMPLATE COMPLEX.

21 AND AS SHOWN ON DNA-V IN THE SCREEN THERE DNA-V COULD
22 THEORETICALLY FOLD BACK ON ITSELF AND FORM A DUPLEX, A SHORT
23 DUPLEX LIKE THAT.

24 Q. NOW, IN DOING THEIR PRIMER EXTENSION REACTIONS ON DNA-V THEY
25 JUST PUT DNA-V INTO A TUBE OBVIOUSLY WITH THE OTHER CHEMICALS

WALLACE-CROSS/PASAHOW

2 1 THAT ARE NECESSARY, BUT THAT WAS THE ONLY DNA THAT WAS IN THERE?

2 A. WHICH EXPERIMENT ARE YOU POINTING TO WHERE?

3 Q. WHEN THEY SHOWED -- WHEN THEY SHOWED DNA-V.

4 A. WHICH FIGURE ARE YOU REFERRING TO?

5 Q. I DIDN'T HAVE A SPECIFIC FIGURE IN MIND.

6 I WANTED TO ESTABLISH AS TO DNA-V ONE OF THE
7 EXPERIMENTS THEY DID WAS HAVE IT PRIME ITSELF AND JUST SHOW THIS
8 END WILL EXTEND DOWN AND FILL IN JUST AS A PRIMER WOULD?

9 A. I HAVE TO LOOK AT THE THE DETAILS. THEY MAY, IN FACT, HAVE
10 HEATED IT IN THE SENSE THEY MAY HAVE ASSEMBLED THE REACTION AT
11 ROOM TEMPERATURE, I DON'T KNOW. THE REACTION WAS PERFORMED AT
12 15 DEGREES. IF YOU'LL LOOK FIGURE 13 WHICH IS THE EXPERIMENT
13 YOU'RE TALKING ABOUT.

14 Q. YOU SAY THEY HEATED IT TO ROOM TEMPERATURE?

15 A. WELL, ROOM TEMPERATURE ABOUT 25 DEGREES CENTIGRADE -- I
16 DON'T KNOW THAT FOR SURE, I HAVE TO LOOK AT HOW HE ASSEMBLED THE
17 REACTION THEN. I HAVEN'T READ THIS PAPER IN SOMETIME AND YOU
18 DON'T KNOW THOSE KINDS OF DETAILS.

19 TYPICALLY IF YOU WERE TO ASSEMBLE A REACTION LIKE
20 THEY'RE TALKING YOU TAKE COMPONENT ONE AND COMPONENT TWO YOU
21 MIGHT COMBINE THEM AT ROOM TEMPERATURE JUST DIFFERENT THE
22 TEMPERATURE OF THE REACTION.

23 Q. WILL THE DNA PIECES COME TOGETHER AT ROOM TEMPERATURE?

24 A. I DON'T KNOW, VERY SHORT DUPLEX, THEY MAY NOT.

25 Q. ANOTHER EXPERIMENT THAT THEY DID WAS TO SEE WHAT WOULD

WALLACE-CROSS/PASAHOW

2
1 HAPPEN IF THEY PUT A PRIMER THAT WOULD PRIME RIGHT IN THIS
2 SECTION HERE; IS THAT RIGHT?

3 A. THAT'S THE FIGURE 13 EXPERIMENT.

4 Q. YES. NOW, WHEN THEY DID THOSE EXPERIMENTS DID THEY HEAT AND
5 COOL?

6 A. AGAIN, I DON'T KNOW HOW THEY ASSEMBLED THIS REACTION. THEY
7 COMBINED THE DNA-V WITH PRIMER AND THEY SAY THEY DID THE
8 REACTION AT 15 DEGREES CENTIGRADE.

9 BUT BASICALLY YOU'RE RIGHT THEY'RE JUST MIXING THEM.
10 WHETHER OR NOT THEY'RE ORIGINALLY AT 25 DEGREES, THEN MOVED TO
11 15 DEGREES, I CAN'T TELL BY QUICKLY LOOKING AT THIS EXPERIMENT.

12 Q. LET ME ASK ONE OTHER QUESTION ABOUT THE STRUCTURES WHILE
13 WE'VE GOT THEM HERE. THE INSTRUCTION DNA-VI WILL THAT EXTEND
14 DOWN THIS WAY?

15 A. SHOULD NOT.

16 Q. WHY IS THAT?

17 A. BECAUSE IT HAS THREE PRIME EXTENSION THERE'S NO PRIME.

18 Q. SO THAT'S WRONG END TO EXTEND FROM?

19 A. HE DESIGNED THAT, I GUESS, AS A CONTROL.

20 Q. NOW, WHEN DOCTOR KLEPPE AND HIS COLLEAGUES DID THE
21 EXPERIMENT WITH THIS FIRST PIECE OF DNA, WHAT WAS THE RATIO OF
22 THE TOP PIECE AND THE BOTTOM PIECE, ONE TO THE OTHER?

23 A. PROBABLY ONE TO ONE.

24 Q. WHEN THEY DID THE EXPERIMENTS WITH THE SECOND PIECE, WHAT
25 WAS THE SECOND PIECE OF THE TOP PIECE TO THE BOTTOM PIECE?

WALLACE-CROSS/PASAHOW

2 1 A. PROBABLY . . . ONE TO ONE. DNA-V EXPERIMENT TALKED ABOUT
2 HAD A DIFFERENT RATIO.

3 Q. LET'S TAKE THEM ONE AT A TIME IF WE COULD. AS TO DNA-III
4 HERE WHAT WAS THE RATIO USED WHEN THEY PUT THOSE TWO IN
5 TOGETHER?

6 A. AGAIN, PROBABLY ONE TO ONE.

7 Q. AND FOR DNA-IV THIS SMALL ONE HERE, WHAT WAS THE RATIO
8 THERE?

9 A. AGAIN, PROBABLY ONE TO ONE. HIS GOAL WAS TO MEASURE
10 COMPLETENESS OF PRIMER EXTENSION, SO THAT WOULD PROBABLY HAVE
11 ABOUT IT.

12 Q. AS TO DNA-V AND DNA-VI HE ACTUALLY USED SEPARATE PRIMERS
13 THAT WEREN'T -- THAT AREN'T IN THIS PICTURE; IS THAT RIGHT?

14 A. YEAH, THAT'S CORRECT.

15 Q. WHEN HE USED THE SEPERATE PRIMERS WHAT WAS HIS RATIO?

16 A. TWO TO ONE IT LOOKS LIKE FROM THE EXPERIMENT THAT I WAS --
17 13, LOOK AT FIGURE 13 THAT WAS TWO TO ONE AND FIGURE 14 WAS TWO
18 TO ONE.

19 Q. SO THE HIGHEST RATIO THAT WAS USED IN THE KLEPPE PAPER WAS
20 TWO TO ONE AND MANY OF THE EXPERIMENTS HE USED ONE TO ONE?

21 A. I BELIEVE.

22 Q. NOW, DO YOU HAVE THE PAPER THAT WAS WRITTEN BY DOCTOR PANET
23 AND DR. KHORANA?

24 A. I DO.

25 Q. THAT'S THE ONE THAT ALSO REFERS TO THE UNPUBLISHED

WALLACE-CROSS/PASAHOW

1 EXPERIMENTS BY DOCTOR MULLINEUX?

2 A. IN THE DISCUSSION THERE IS A REFERENCE TO THE SUCCESSFUL
3 EXPERIMENTS OF DOCTOR MULLINEUX, YES.

4 Q. NOW, IN THE DISCUSSION OF THE WORK THAT DOCTOR PANET DID
5 WHERE HE TELLS US THE DETAILS OF HOW HE DID THE EXPERIMENTS,
6 WHAT WAS HIS PRIMER TO THE TEMPLATE RATIO?

7 A. IN THE EXPERIMENTS IN THE PAPER?

8 Q. YEAH.

9 A. OR THE EXPERIMENTS IN THE DISCUSSION --

10 Q. THE DETAILED --

11 A. -- I WAS JUST DESCRIBING?

12 Q. THE DETAILED EXPERIMENTS THAT DOCTOR PANET HIMSELF DID AND
13 LAYS OUT THE REACTION CONDITIONS.

14 A. I FORGOTTEN THE EXACT RATIOS. THEY WERE PROBABLY LESS . . .
15 THEY WERE PROBABLY TWO TO ONE OR ONE TO ONE. I CAN'T FIND IT ON
16 QUICK REVIEW. AND IN THE DISCUSSION HE RECOMMENDS TEN TIMES OR
17 MORE IN THAT PARAGRAPH WE WERE TALKING ABOUT.

18 Q. THAT IS THE DISCUSSION OF THE WORK DONE BY DOCTOR MULLINEUX
19 THAT TALKS ABOUT TEN TO ONE?

20 A. TIMES OR MORE.

21 Q. SO THE HIGHEST THAT IS REFERRED TO IN THAT ARTICLE, AT
22 LEAST, IS TEN OR MORE TO ONE?

23 A. TEN OR MORE.

24 Q. DO YOU RECALL IF THE NATIONAL SCIENCE FOUNDATION DESCRIPTION
25 TELLS US WHAT THE RATIO IS?

WALLACE-CROSS/PASAHOW

3
1 A. I BELIEVE IT SAYS . . . EXCESS.

2 Q. EXCESS?

3 A. IN EXCESS.

4 Q. SO THAT'S ANYTHING MORE THAN ONE TO ONE?

5 A. MORE THAN ONE TO ONE.

6 Q. NOW, YOU ALSO REFERRED US TO SOME EXPERIMENTS THAT WERE DONE
7 IN 1984 INVOLVING PRIMERS AND TEMPLATES IN YOUR TESTIMONY, AND
8 ONE OF THOSE WAS YOUR PAPER WHICH WAS LABELED B-148. DO YOU
9 HAVE THAT UP THERE? THIS IS THE REAL SPECIFIC HYBRIDIZATION
10 PAPER.

11 A. BURIED IN HERE SOMEWHERE. YES.

12 Q. WHAT RATIO DID YOU USE IN THAT PAPER?

13 A. IT'S ABOUT THREE TO ONE.

14 Q. THREE TO ONE.

15 A. YES.

16 Q. AND YOU ALSO TOLD US ABOUT YOUR PAPER INVOLVING DOUBLE
17 STRANDED SEQUENCING WHICH WE MARKED AS EXHIBIT A-47. DO YOU
18 HAVE THAT?

19 A. YES.

20 Q. WHAT WAS THE RATIO OF PRIMERS TO THE TEMPLATE IN THAT PAPER?

21 A. 20 TO ONE.

22 Q. 20 TO ONE, WE'RE UP TO 20 TO ONE.

23 NOW, DO YOU RECALL IF ANY OF THE HONG PAPERS TOLD US
24 WHAT THE PRIMER TO THE TEMPLATE RATIO WAS?

25 A. I DON'T RECALL. PART OF THE PROTOCOL, I DON'T RECALL OFF

WALLACE-CROSS/PASAHOW

3
1 THE TOP OF MY HEAD.

2 Q. WOULD YOU TAKE A LOOK AND SEE IF YOU CAN DETERMINE IT?

3 A. WHICH NUMBERS ARE THOSE?

4 Q. A-109 AND A-110.

5 (PAUSE IN THE PROCEEDINGS)

6 THE WITNESS: I DON'T SEE IT OFF THE TOP OF MY HEAD.
7 OFTEN WITH M13 SEQUENCING YOU DON'T KNOW THE TEMPLATE
8 CONCENTRATION. IT MAY BE IT'S NOT LISTED. FOR THAT REASON AND
9 I DIDN'T FIND IT ON 110. TYPICALLY FOR A SEQUENCING REACTION
10 IT'S IN EXCESS OF AROUND 20 TO ONE.

11 (PAUSE IN THE PROCEEDINGS)

12 THE WITNESS: WELL, I CAN'T TELL WITH THE A-110 BECAUSE
13 HE SAYS THAT THE DNA WAS DONE ACCORDING TO ANOTHER REFERENCE
14 WHICH I DON'T HAVE IN FRONT OF ME. PREPARED ACCORDING TO SANGER
15 EXCEPT THE DNA WAS DISSOLVED IN 25 MICROLITERS, SO IT MAY BE
16 THAT HE USES POINT TWO PICOMOLES PER MICROLITER. BUT IT DOESN'T
17 SAY DNA CONCENTRATIONS, AS FAR AS I CAN SEE.

18 Q. (BY MR. PASAHOW) NOW, YOU TOLD US YESTERDAY THAT CLAIM 15
19 OF THE '202 PATENT WHICH CALLS FOR A MOLAR RATIO OF AT LEAST
20 1,000 TO ONE OF THE PRIMER TO THE COMPLIMENTARY STRAND IS FOUND
21 IN THIS PRIOR ART?

22 A. NO, I DIDN'T SAY THAT. I SAID THAT IF YOU WERE GOING TO
23 ATTEMPT TO AMPLIFY SOMETHING, WHICH IS YOUR GOAL, THEN YOU WOULD
24 KNOW HOW MUCH PRIMER TO USE, PRIMER EXTENSIONS COMSUME PRIMER.
25 EVERY CYCLE MOLECULE OF A PRIMER EXTENSION REACTION THE PRODUCTS

WALLACE-CROSS/PASAHOW

3
1 HAS A PRIMER IN IT.

2 Q. SO IF I WAS DOING THE TWO CYCLES CALLED FOR BY CLAIM 1 I
3 WOULD NEED FOUR PRIMERS; IS THAT RIGHT?

4 A. THE TWO CYCLES OF CLAIM 1 CONSUMES FOUR PRIMERS. WELL,
5 ACTUALLY EIGHT PRIMERS, FOUR PRIMERS ON EACH STRAND. IS THAT
6 RIGHT? FOUR PRIMERS.

7 Q. IN THE RATIO NUMBERS WE'RE TALKING ABOUT THEY MEAN THE RATIO
8 OF EACH TYPE OF PRIMER TO THE TEMPLATE, ISN'T THAT RIGHT?

9 A. THAT'S CORRECT.

10 Q. SO FOR CLAIM 1 WOULD BE A RATIO OF FOUR TO ONE BE NECESSARY
11 FOR EACH STRAND TO HAVE A PRIMER?

12 A. RIGHT.

13 Q. AND IF I DO IT ONE MORE TIME TO DO CLAIM 2 THEN I WOULD NEED
14 EIGHT PRIMERS; IS THAT RIGHT?

15 A. THAT'S CORRECT.

16 Q. SO IF A SCIENTISTS USE THAT KIND OF THINKING HE REALIZED HE
17 NEEDED EIGHT PRIMERS TO DO THE REACTION CALLED FOR BY CLAIM 2?

18 A. AT LEAST EIGHT PRIMERS WOULD BE CONSUMED BY CLAIM 2,
19 ASSUMING IT'S A HUNDRED PERCENT EFFICIENT.

20 Q. WHERE WOULD THE ORDINARY SKILLED PERSON IN 1984 GO TO FIND
21 OUT THAT HE NEEDED MORE THAN 1,000 TO ONE AS IS CALLED FOR BY
22 CLAIM 15?

23 A. WELL, I WAS JUST COMMON SENSE IF YOU'RE GOING TO MAKE 1,000
24 TIMES, 1,000 COPIES OF SOMETHING YOU NEED 1,000 PRIMERS.

25 Q. BUT THIS IS 1,000 PRIMERS, MORE THAN 1,000 PRIMERS TO DO

WALLACE-CROSS/PASAHOW

4
1 CLAIM 1, ISN'T THAT RIGHT?

2 A. CLAIM 1 DOESN'T ASK YOU TO DO MORE THAN TWO CYCLES.

3 Q. SO WHAT CLAIM 15 PROVIDES, YOU UNDERSTAND, IS THAT YOU USE
4 MORE THAN 1,000 TO ONE PRIMERS TO THE TEMPLATE IN ORDER TO DO
5 THE TWO CYCLES OF CLAIM 1?

6 A. UH-HUH.

7 Q. IS THAT CORRECT?

8 A. YES, THAT WOULD BE ONE. YES, I SEE WHAT WHAT YOU'RE SAYING,
9 YES.

10 Q. SO WHERE WOULD A SCIENTISTS OF ORDINARY SKILL IN 1984 GO TO
11 LEARN THAT HE SHOULD USE MORE THAN 1,000 TO ONE PRIMER TO THE
12 TEMPLATE IN ORDER TO MAKE EIGHT COPIES?

13 A. I GUESS I DON'T FULLY UNDERSTAND HOW THAT GOT -- CLAIM GOT
14 IN THERE THEN BECAUSE THE SPECIFICATION DOESN'T TEACH YOU THAT
15 EITHER.

16 Q. DO YOU HAVE THE PATENT IN FRONT OF YOU THERE?

17 A. PROBABLY. THIS PILE IS GETTING SO HIGH IT'S HARD TO FIND.

18 Q. THEY HAVE THE BLUE RIBBONS, IF THAT HELPS.

19 A. YES.

20 Q. COULD YOU TURN TO COLUMN 15 AND EXAMPLE ONE AND CONFIRM FOR
21 ME THAT THAT EXAMPLE USES 1,000 TO ONE PRIMER TO THE TEMPLATE?

22 A. THAT'S TRUE. EXAMPLE ONE USES 14 ROUNDS OF PCR AND I
23 DON'T -- AGAIN, I MEAN, IT'S NOT ADDING THOUSAND TO ONE TO DO
24 TWO ROUNDS OF PCR, IT'S ADDING THOUSAND TO ONE TO DO 14 ROUNDS
25 OF PCR, SO IT'S COMMON SENSE, IF THE REACTION IS WORKING IT'S

WALLACE-CROSS/PASAHOW

1 GOING TO CONSUME THE PRIMER.

2 Q. IF I STARTED OUT DOING EXPERIMENT -- THE EXPERIMENT THAT'S
3 IN EXAMPLE ONE, THE FIRST TWO CYCLES OF THAT EXAMPLE WOULD BE
4 CLAIM 1 OF THE PATENT; IS THAT RIGHT?

5 A. RIGHT.

6 Q. AND BECAUSE I START OUT WITH MORE THAN 1,000 TO ONE PRIMER
7 TO THE TEMPLATE THEY WOULD ALSO CONSTITUTE A PROCESS WHICH IS
8 COVERED BY CLAIM 15; IS THAT RIGHT?

9 A. I GUESS, THE LAST FEW CYCLES WOULDN'T HAVE ANY PRIMER IN
10 THEM.

11 Q. IF IT WENT INTO HUNDRED PERCENT EFFICIENCY?

12 A. I SUPPOSE, YEAH. ALL I'M SAYING, IF YOUR GOAL WAS TO
13 MAKE -- OKAY, MY TESTIMONY WAS THAT IF YOUR GOAL WAS TO DO TEN
14 TIMES WHICH WOULD BE ABOUT A THOUSAND TIMES AMPLIFICATION, YOU
15 MIGHT THINK IT'S LOGICAL TO HAVE 1,000 TO ONE, BUT NOT LOGICAL
16 TO ADD THOUSAND TO ONE TO DO TWO CYCLES.

17 Q. WHEN YOU DO PCR IN YOUR LABORATORY ON HUMAN DNA YOU USE
18 RATIOS LIKE A MILLION TO ONE?

19 A. THAT'S ONE OF THE PARAMETERS WE VARY ALL OVER THE PLACE. I
20 DON'T KNOW EXACTLY WHAT WE USE. IT'S AN IMPORTANT PARAMETER IN
21 PCR.

22 Q. IN THE PANET AND KLEPPE PAPERS WERE ANY OF THE EXPERIMENTS
23 DONE USING KLENOW?

24 A. NO, I DON'T BELIEVE SO.

25 Q. IN KLENOW YOU EXPLAINED IS THIS MORE REFINED PORTION OF THE

WALLACE-CROSS/PASAHOW

1 DNA POLYMERASE 1; IS THAT RIGHT?

2 A. NO, NOT REALLY MORE REFINED. IT WAS SORT OF DEGRADED
3 VERSION OF IT ACTUALLY, REMOVED AN ACTIVITY.

4 Q. IT'S DERIVED FROM DNA POLYMERASE 1?

5 A. DERIVED FROM.

6 Q. YOU TOLD MR. FIGG THAT THE 1984 SCIENTISTS WOULD USE KLENOW
7 INSTEAD OF THE ENZYMES THAT ARE REFERRED TO IN KLEPPE AND PANET
8 IN GOING ABOUT DOING THIS REACTION?

9 A. I THINK I TESTIFIED TO 1984.

10 Q. I MISSPOKE IF I SAID SOME OTHER DATE. I MEANT TO SAY 1984.

11 SO TO TRY TO MAKE THAT POINT MORE CLEARLY, IN 1984 IT'S
12 YOUR BELIEF THAT A SCIENTISTS WOULD USE SOME POLYMERASE OTHER
13 THAN THE ONE THAT'S REFERRED TO IN THE PANET AND KLEPPE PAPERS,
14 IN THE NATIONAL SCIENCE FOUNDATION GRANT?

15 A. YOU WOULD HAVE LIKELY TURNED TO THE KLENOW ENZYME YOU, COULD
16 BUY IT, IT WAS USED FOR SEQUENCING. PROBABLY PREFER TO USE THAT
17 ENZYME.

18 Q. NOW, THESE DIFFERENT ENZYMES THEY HAVE THEIR OWN CHEMICALS
19 THAT GO WITH THEM THAT THEY WORK BEST WITH; IS THAT RIGHT?

20 A. WHICH DIFFERENT POLYMERASE ENZYMES?

21 Q. FOR EXAMPLE, IF YOU WENT TO USE KLENOW INSTEAD OF THE FOUR
22 POLYMERASE THAT WAS USED IN SOME OF THE EXPERIMENTS, YOU USE A
23 REACTION MIX THAT YOU THOUGHT WOULD WORK WELL WITH THE KLENOW?

24 A. IF YOU'RE USING KLENOW, YES, YOU MIGHT HAVE FOUND A
25 PARTICULAR SET OF CONDITIONS WORKED BETTER FOR ONE ENZYME THAN

WALLACE-CROSS/PASAHOW

5
1 ANOTHER ENZYME.

2 Q. AND THERE ARE PUBLISHED RECIPES FOR THOSE KIND OF
3 CONDITIONS?

4 A. FOR SOME OF THE ENZYMES, YES.

5 Q. ARE PUBLISHED RECIPES FOR KLENOW; IS THAT RIGHT?

6 A. YES.

7 Q. THEY WERE IN 1984?

8 A. YES.

9 Q. IN FACT, WHEN YOU BOUGHT KLENOW ONE OF THOSE RECIPES
10 GENERALLY ACCOMPANIED IT; IS THAT RIGHT?

11 A. THAT'S CORRECT.

12 Q. AND IS IT YOUR BELIEF, THAT THE ORDINARILY SKILLED PERSON IN
13 19884 COULD HAVE USED THE CONDITIONS THAT WERE PUBLISHED FOR
14 USING KLENOW IN TRYING TO DO THIS TYPE OF REACTION?

15 A. IT DEPENDS ON WHAT THEIR OWN EXPERIENCE WITH THE ENZYME WAS.
16 I, FOR EXAMPLE, DON'T BELIEVE I USED THE CONDITIONS THAT WERE
17 SUPPLIED WITH THE ENZYME WHEN I USE KLENOW.

18 Q. WHAT YOU'RE SAYING IS, HAVE YOUR OWN FAVORITE RECIPES FOR
19 THE CONDITIONS OF KLENOW?

20 A. I'M SAYING I MIGHT HAVE CHOSEN SOMEBODY ELSE'S PRIOR --
21 USUALLY YOU GO TO A REFERENCE AND SOMEBODY USED THIS
22 COMPOSITION, SOMEBODY USES THAT, IT'S NOT JUST ONE.

23 Q. IT'S YOUR BELIEF THAT THE ORDINARILY SKILLED PERSON IN 1984
24 WOULD HAVE GONE TO ONE OF THESE REFERENCES FOR RECIPE FOR USE
25 WITH KLENOW RATHER THAN USE THE RECIPES THAT ARE IN THE PANET OR

WALLACE-CROSS/PASAHOW

1 KLEPPE PAPERS; IS THAT RIGHT?

2 A. THEY LIKELY WOULD HAVE USED CONDITIONS WHICH THEY KNEW
3 WORKED IN THEIR HANDS. I'M ASSUMING THIS PERSON WOULD HAVE BEEN
4 DOING KLENOW REACTIONS.

5 Q. AND THEY WOULD HAVE USED CONDITIONS THEY FOUND IN SOME
6 REFERENCE THAT WAS RELATIVELY MODERN IN 1984 AND WAS SET UP FOR
7 USING KLENOW?

8 A. WELL, YOU KNOW, IT'S A HYPOTHETICAL SITUATION. I DON'T KNOW
9 IF THEY READ KLEPPE THEY MIGHT HAVE TRIED THAT RECIPE, TOO. YOU
10 WOULD NORMALLY HAVE LOOKED IN THE LITERATURE AND USED WHAT WAS
11 CONSIDERED TO BE BEST FOR THAT PARTICULAR ENZYME.

12 Q. WHEN DO YOU FIRST RECALL ACTUALLY READING KLEPPE?

13 A. I HAVE TROUBLE WITH THIS BEFORE, IT WAS LAST YEAR.

14 Q. WHO CALLED IT TO YOUR ATTENTION?

15 A. MR. FIGG SENT ME THE COPIES OF THE PATENTS AND THE
16 REFERENCES AND I READ THEM, AND WAS AFTER READING THEM THAT I
17 FORMED MY OPINIONS.

18 Q. SO YOUR MODERN RECOLLECTION OF THESE ARTICLES, AT LEAST,
19 COMES FROM BEING SENT THE ARTICLES BY DU PONT'S LAWYERS?

20 A. THAT'S CORRECT.

21 Q. ONE LAST THING. YOU GAVE SOME TESTIMONY YESTERDAY ABOUT A
22 DECLARATION THAT DOCTOR HENRY ERLICH FILED IN THE PATENT OFFICE,
23 DO YOU RECALL THAT?

24 A. YES.

25 Q. AND YOU TOLD US THAT THIS AFFIDAVIT WAS FILED IN RESPONSE TO

WALLACE-CROSS/PASAHOW

5 1 A REJECTION FROM THE PATENT EXAMINER?

2 A. AS I UNDERSTOOD IT, IT WAS FILED IN RESPONSE TO REJECTION OF
3 CLAIM 14 AND WAS, I GUESS, DESIGNED TO SHOW THAT CLAIM 14 COULD
4 BE MADE TO WORK.

5 Q. NOW, YOU TOLD US YESTERDAY THAT YOU THOUGHT THAT IT WAS
6 FILED FOR THE PURPOSE OF SHOWING WHAT ONE ORDINARILY SKILLED IN
7 THE ART WOULD KNOW IN 1984, IS THAT STILL YOUR BELIEF?

8 A. WELL, I BELIEVE THAT IF IT WAS FILED -- IF THAT PERSON WAS
9 DOING THOSE EXPERIMENTS WAS MORE THAN ORDINARY SKILLED IT
10 WOULDN'T HAVE SUPPORTED A CLAIM THAT WAS -- WOULDN'T HAVE
11 SUPPORTED THE CLAIM.

12 Q. WELL, COULD YOU READ TO US THE LANGUAGE FROM THE AFFIDAVIT
13 OR DECLARATION THAT YOU BELIEVE INDICATES THAT SOMEONE IS SAYING
14 WHAT ONE ORDINARILY SKILLED IN 1984 COULD DO?

15 A. CAN YOU TELL ME THE NUMBER?

16 Q. OF COURSE. IT'S EXHIBIT A-99.

17 (PAUSE IN THE PROCEEDINGS)

18 THE WITNESS: THE DECLARATION BASICALLY SAYS THAT THE
19 APPENDED MATERIAL DEMONSTRATED THAT CLAIM 14 WORKED. AND IT
20 SAYS THAT IT WAS WORK DONE BY FRED FALOONA, A TECHNICIAN OF
21 DOCTOR KARY MULLIS ACTING UNDER DR. MULLIS' IMMEDIATE
22 SUPERVISION AND MY OVERALL DIRECTION.

23 Q. (BY MR. PASAHOW) DR. WALLACE, I WAS ASKING YOU TO PLEASE
24 READ THE LANGUAGE WHICH YOU BELIEVE INDICATES THAT DOCTOR HENRY
25 ERLICH WAS TELLING THE PATENT OFFICE WHAT ONE ORDINARILY SKILLED

WALLACE-CROSS/PASAHOW

6 1 IN 1984 COULD DO.

2 A. I WAS JUST DRAWING THE CONCLUSION THAT THAT'S WHAT THE --
3 WHAT THE INFERENCE WAS, FROM THE FACT THAT A TECHNICIAN
4 PERFORMED THIS UNDER DOCTOR MULLIS' DIRECTION.

5 Q. DR. MULLIS IS THE INVENTOR OF PCR?

6 A. THAT'S TRUE. EXCUSE ME, THAT ISN'T TRUE. THAT'S TRUE,
7 THAT'S WHAT HE WAS TELLING THE PATENT OFFICE, DR. MULLIS WAS THE
8 NAMED INVENTOR ON THIS APPLICATION, BUT SINCE I JUST ASSUMED
9 THAT THE DECLARATION WAS MEANT TO SUPPORT THAT ANYBODY COULD DO
10 IT.

11 Q. DOES THE DECLARATION SAY ANYWHERE ONE --

12 A. DOESN'T SAY THAT. IN CONCLUSION THE EXPERIMENTS CONDUCTED
13 BY FRED FALOONA AND EVIDENCE BY APPENDIX B DEMONSTRATE THE
14 APPLICATION OF VARIOUS DNA SEGMENTS CAN BE CARRIED OUT USING A
15 HEAT STABLIZED ENZYME CONSTANT ELEVATED TEMPERATURE ANNEALING
16 AND SEPARATION STEPS IN ACCORDANCE WITH CLAIM 14 OF THE ABOVE
17 IDENTIFIED APPLICATION.

18 Q. NOW, YOU ALSO TOLD US YESTERDAY THAT IT WAS YOUR BELIEF THAT
19 THE POINT OF THE ARGUMENT DR. ERLICH MADE WAS THAT THE CONCEPTS
20 OF PCR WERE TAUGHT BY CLAIM 1, AND THAT ONCE YOU UNDERSTOOD THAT
21 YOU SHOULD BE ABLE TO DO THE PROCESS OF CLAIM 14 THROUGH
22 ORDINARY EXPERIMENTATION, TESTING OF CONDITIONS FOR THIS
23 REACTION AND GETTING IT TO WORK.

24 CAN YOU TELL ME PLEASE WHAT LANGUAGE IN THE DECLARATION
25 YOU BELIEVE SAYS THAT?

WALLACE-CROSS/PASAHOW

6 1 A. WHAT THE DECLARATION IS SAYING IS THAT IT WORKED. IT WAS MY
2 ASSUMPTION IT WAS NECESSARY TO DEMONSTRATE TO THE PATENT OFFICE
3 THAT IT COULD BE MADE TO WORK BY ONE OF ORDINARY SKILL.

4 Q. WHAT WAS THAT ASSUMPTION BASED ON?

5 A. BASED ON THE FACT THAT THERE WAS NO SPECIFICATION DESCRIBING
6 A THERMOSTABLE ENZYME AND I THOUGHT THAT THAT MEANT THAT THE
7 CLAIM WASN'T SUPPORTED BY THE SPECIFICATION. JUST MY OWN
8 INTERPRETATION OF IT.

9 Q. YOU ALSO TOLD US YESTERDAY THAT MR. FALOONA IN HIS
10 EXPERIMENTS USED A CHEMICAL THAT YOU ABBREVIATED AS BSA?

11 A. BSA, THAT'S CORRECT.

12 Q. AND I THINK YOU TOLD US ALSO THAT THAT WASN'T REFERRED TO IN
13 THE PATENT EXAMPLES?

14 A. I THINK IT WAS IN SOME OF THE RESTRICTION ENZYME DIGESTERS
15 BUFFERS, BUT I DON'T RECALL IT. I THINK I SAID I DIDN'T RECALL
16 IT BEING IN THE BUFFERS WHICH MADE UP THE AMPLIFICATION REACTION
17 MIX. I MAY BE WRONG.

18 Q. FINALLY YOU TOLD US YESTERDAY THAT MR. FALOONA HAD TO WAIT
19 DAYS TO MAKE THIS REACTION WORK AND THAT WAS OUTSIDE THE
20 PARAMETERS OF THE EXAMPLES IN THE PATENT WHICH WERE DONE IN
21 HOURS?

22 A. NO, I DIDN'T SAY THAT.

23 MR. FIGG: THAT MISCHARACTERIZES DR. WALLACE'S PREVIOUS
24 TESTIMONY.

25 THE COURT: REPHRASE YOUR QUESTION.

WALLACE-CROSS/PASAHOW

MR. PASAHOW: YES.

Q. LET ME REVIEW WITH YOU, PLEASE, THE TESTIMONY YOU DID GIVE. MR. FIGG ASKED, WERE THERE ANY CONSTRAINTS IN THE EXPERIMENTS DESCRIBED IN THE DECLARATION, ANY CONSTRAINTS WITH REGARD TO THE LENGTH OF TIME THE REACTION WAS ALLOWED TO PROCEED?

AND YOU ANSWERED THE TIME OF THE REACTION WAS THE REACTION WAS CARRIED OUT FOR VARIOUS LENGTHS OF TIME. BUT THE REACTION WORKED, FOR EXAMPLE, FOR ONE PARTICULAR EXAMPLE THEY HAD TO CARRY OUT THE REACTION FOR ONE DAY AND FOR SEVEN DAYS, SO THE REACTION TIME WAS CHANGED FROM HOURS TO DAYS AND AS LONG AS SEVEN DAYS IN SOME CASES.

NOW, THE EXPERIMENTS THAT MR. ERLICH ATTACHED SHOWED THAT THE REACTION WORKED WITHIN HOURS, ISN'T THAT RIGHT?

A. THAT'S WHAT HE SAID, WITHIN HOURS AND UP TO SEVEN DAYS.

Q. SO HE WAS SHOWING IT WORKED THROUGHOUT THAT TIME PERIOD?

A. SHOWED THE TIME WAS IMPORTANT.

Q. IT WORKED AS WELL IN A FEW HOURS AS IT DID OVER SEVERAL DAYS?

A. I DON'T KNOW. IT SAID . . . IT SAID FOR ONE DAY AND FOR SEVEN DAYS IN THE CASE OF THE '75, THAT'S WHAT THE AFFIDAVIT STATED.

Q. BUT YOU LOOKED AT THE EXPERIMENTS AS WELL?

A. YES, I HAVE LOOKED.

Q. THEY SLOWED THE REACTION WORKED WELL WITHIN ONE HOUR?

A. IT WORKED WITHIN ONE HOUR IN SOME CASES, I THINK.

WALLACE-REDIRECT/FIGG

1 MR. PASAHOW: I HAVE NOTHING ELSE, YOUR HONOR.

2 THE COURT: OKAY. MR. FIGG.

3 REDIRECT EXAMINATION

4 MR. FIGG: DR. WALLACE, AS MR. PASAHOW POINTED OUT YOU
5 GOT SOME PATENT APPLICATIONS OF YOUR OWN. DEALING WITH THAT
6 LAST SUBJECT THAT MR. PASAHOW WAS COVERING WITH YOU, WHAT DO YOU
7 UNDERSTAND THE PURPOSE OF THE SPECIFICATION OF YOUR PATENT
8 APPLICATIONS TO BE?

9 A. WELL, I PRESUME THAT IT WILL TEACH THE BEST WAY TO YOUR
10 KNOWLEDGE TO DO THE EXPERIMENTS DESCRIBED BY THE CLAIM.

11 Q. TO WHOM IS THAT SPECIFICATION DIRECTED, DO YOU HAVE ANY
12 UNDERSTANDING OF THAT?

13 A. IT'S MY UNDERSTANDING TO ONE OF ORDINARY SKILL IN THE ART.

14 Q. AND WHY DO YOU UNDERSTAND OR DO YOU HAVE AN UNDERSTANDING OF
15 WHY THE PATENT EXAMINER REJECTED CLAIM 14 OF THE CETUS PATENT
16 APPLICATION?

17 A. WELL, AS I SAID, IT WAS MY OPINION THAT, OR MY UNDERSTANDING
18 THAT IT WAS BECAUSE THE SPECIFICATION DIDN'T SUPPORT THE CLAIM.

19 Q. EVEN WHEN YOU SAY --

20 A. IN OTHER WORDS, ONE OF ORDINARY SKILL IN THE ART COULD NOT
21 HAVE PERFORMED CLAIM 14 WITHOUT THE NECESSARY SPECIFICATION.

22 Q. AND CETUS PRESENTED THE EVIDENCE THAT SINCE DR. MULLIS AND
23 DOCTOR FALOONA COULD DO IT, PERSON OF ORDINARY SKILL COULD DO
24 IT, ISN'T THAT CORRECT?

25 A. THAT'S HOW I INTERPRETED THAT, YES.

WALLACE-REDIRECT/FIGG

7
1 Q. SO CETUS WAS ACTUALLY EQUATING DR. MULLIS AND DOCTOR FALOONA
2 WITH A PERSON OF ORDINARY SKILL IN THE ART?

3 A. THAT'S HOW I INTERPRETED IT, YES.

4 Q. DOCTOR PASAHOW -- OR MR. PASAHOW WAS ASKING YOU ABOUT YOUR
5 PATENT APPLICATION ON DEVELOPING A TEST FOR DIAGNOSING HIV
6 INFECTIONS, THE AIDS INFECTION, DO YOU RECALL THAT?

7 A. YES.

8 Q. NOW, WHEN YOU FILED THAT PATENT APPLICATION DID YOU KNOW OF
9 ANY OF THE THREE PIECES OF THE KHORANA PRIOR ART THAT WE'VE BEEN
10 TALKING ABOUT HERE?

11 A. NO, I DID NOT.

12 Q. AND YOU HAD YOU EVER SEEN THE CETUS '195?

13 A. NO, I HAD NOT.

14 Q. OR THE CETUS '202 PATENT?

15 A. NO, I HAD NOT.

16 Q. HAD YOU EVER SEEN -- YOU SAID YOU SEEN ONE PAPER THAT COME
17 FROM CETUS THAT WAS THE SAIKI PAPER?

18 A. THAT'S THE PAPER THAT COMES TO MIND.

19 Q. AND YOUR PATENT APPLICATION WAS DIRECTED TO A METHOD OF
20 AMPLIFYING RNA AND THEN DETECTING THE AMPLIFICATION PRODUCT; IS
21 THAT RIGHT?

22 A. THAT'S CORRECT.

23 Q. AND THE AIDS VIRUS IS A VIRUS THAT CONTAINS RNA?

24 A. YEAH, I THINK I SAID PREVIOUSLY THE ORGANISMS CONTAINED
25 NUCLEIC ACIDS, EITHER DNA OR RNA. THE HIV ONE VIRUS CALLED A

WALLACE-REDIRECT/FIGG

7
1 RETRO-VIRUS CONTAINS AN RNA, SO WE WERE DEVELOPING A METHOD TO
2 TEST FOR THAT RNA, THAT SPECIFIC RNA.

3 Q. DID THE SAIKI PAPERS SAY ANYTHING ABOUT AMPLIFYING RNA AND
4 DETECTING IT FOR THE PURPOSE OF DIAGNOSING VIRAL DISEASE?

5 A. NO, I DON'T THINK IT DID.

6 Q. NOW, SOMETIME AFTER YOU FILED THAT PATENT APPLICATION DID
7 THE '195 PATENT AND '202 PATENT ISSUE?

8 A. YES, THEY DID.

9 Q. AND DO THOSE PATENTS SAY ANYTHING ABOUT AMPLIFYING RNA?

10 A. REVERSE TRANSCRIPTASE IS MENTIONED IN THE CLAIMS AS A WAY OF
11 CONVERTING RNA TO DNA.

12 Q. AND SO WHAT DID YOU DO AFTER THAT LATER DISCOVERED PRIOR ART
13 CAME OUT, WHAT DID YOU DO IN CONNECTION WITH YOUR PATENT
14 APPLICATION?

15 A. PATENT APPLICATION BEEN ABANDONED.

16 Q. NOW, MR. PASAHOW POINTED OUT THAT YOU REFILED THAT PATENT
17 APPLICATION . . . DO YOU RECALL WHETHER OR NOT THE RECLAIMS OF
18 THAT REFILED APPLICATION -- WHETHER THAT CLAIM THAT MR. PASAHOW
19 WAS REFERRING TO STILL EXISTS IN THAT PATENT APPLICATION THAT
20 WAS REFILED?

21 A. I THINK THE CLAIM HAS SINCE BEEN DROPPED.

22 Q. LET ME SHOW YOU A DOCUMENT THAT WE WILL MARK OR HAVE MARKED
23 AS EXHIBIT A-170.

24 I'M NOT SURE WHAT THE PROCEDURE HERE IS, YOUR HONOR, DO
25 WE NEED A STICKER BEFORE WE SHOW IT TO THE WITNESS?

WALLACE-REDIRECT/FIGG

7
1 THE COURT: TECHNICALLY. BUT IT'S ALWAYS A GOOD IDEA
2 TO MAKE SURE IT'S THERE.

3 THE CLERK: PLAINTIFFS A-170 MARKED FOR IDENTIFICATION.

4 (PLAINTIFF'S EXHIBIT 170

5 MARKED FOR IDENTIFICATION)

6 MR. FIGG: THANK YOU.

7 Q. DO YOU RECOGNIZE THIS AS AN AMENDMENT THAT WAS FILED WITH
8 YOUR PATENT APPLICATION?

9 A. IT IS AN AMENDMENT OF THAT PATENT APPLICATION.

10 Q. WHAT IS THE FIRST INSTRUCTION IN THAT AMENDMENT TO THE
11 PATENT OFFICE?

12 A. IT SAYS, PLEASE CANCEL CLAIM 1, THE ONLY PENDING CLAIM, AND
13 ADD THE FOLLOWING NEW CLAIMS.

14 Q. ARE THE FOLLOWING NEW CLAIMS MORE SPECIFIC THAN CLAIM 1 WAS?

15 A. YES, THEY ARE. THEY DEAL WITH LOOKING AT VIRUSES
16 SPECIFICALLY AND SPECIFIC DIAGNOSIS OF VIRUSES WHICH CAUSE HUMAN
17 DISEASE.

18 Q. AND WHAT IS THE TITLE OF THIS DOCUMENT HERE?

19 A. AMENDMENT BEFORE ACTION.

20 Q. SO, IN FACT, YOU'RE ASKING THE PATENT OFFICE TO MAKE THAT
21 AMENDMENT BEFORE THEY EVEN START LOOKING AT YOUR NEW PATENT
22 APPLICATION?

23 A. THAT'S WHAT I ASSUME IT MEANS. I DON'T KNOW WHAT THESE
24 PROCEDURES ARE.

25 Q. OKAY. NOW, MR. PASAHOW ASKED YOU ABOUT THE CITY OF HOPE

WALLACE-REDIRECT/FIGG

8 1 HAVING PATENT APPLICATIONS THAT INVOLVE THE USE OF PCR, THE CITY
2 OF HOPE AND YOU IN PARTICULAR ALSO HAVE PATENT APPLICATIONS ON
3 ON OTHER WAYS OF AMPLIFYING DNA, ISN'T THAT RIGHT?

4 A. THAT'S CORRECT.

5 Q. WHAT DO YOU THINK THE IMPACT OF THE CETUS PATENTS BEING HELD
6 INVALID WOULD HAVE ON THE VALUE OF THE PATENTS ON THE OTHER WAYS
7 OF AMPLIFYING DNA?

8 A. WELL, IT'S HARD TO SAY, BUT IT'S SORT OF IRONIC THAT IF THE
9 CETUS PATENTS WERE FOUND INVALID, MY METHODS OF AMPLIFICATION
10 WHICH -- FOR WHICH WE'VE APPLIED PATENTS BECOME LESS VALUABLE
11 BECAUSE PEOPLE COULD PRACTICE PCR.

12 Q. DO YOU RECALL MR. PASAHOW ASKING YOU SOME QUESTIONS ABOUT
13 WHETHER YOU CITED THE KLEPPE PAPER AND PANET PAPER AND SO FORTH
14 TO THE PATENT AND TRADEMARK OFFICE IN CONNECTION WITH YOUR
15 PATENT APPLICATIONS?

16 A. I DO.

17 Q. DO YOU BELIEVE THAT -- LET ME BACK UP.

18 IS IT YOUR UNDERSTANDING THAT YOUR DUTY TO CITE THIS
19 KIND OF PRIOR ART TO THE PATENT OFFICE MEANS THAT YOU HAVE TO
20 CITE MORE THAN ONE REFERENCE THAT TEACHES THE SAME THING?

21 MR. PASAHOW: EXCUSE ME, YOUR HONOR, MR. FIGG IS
22 LEADING HIS WITNESS.

23 THE COURT: OBJECTION IS SUSTAINED.

24 MR. FIGG: I WILL WITHDRAW IT, YOUR HONOR.

25 Q. DR. WALLACE, WHAT IS YOUR UNDERSTANDING ABOUT THE

WALLACE-REDIRECT/FIGG

8 1 REQUIREMENT TO CITE PRIOR ART THAT TEACHES THE SAME THING AS
2 ANOTHER PIECE OF PRIOR ART THAT HAS ALREADY BEEN CITED TO THE
3 PATENT AND TRADEMARK OFFICE?

4 A. WELL, MY UNDERSTANDING IS THAT YOU WOULD CITE THE MOST
5 RECENT, FOR EXAMPLE, OR AN EXAMPLE OF THE PRIOR ART. AN
6 ARTICLE, FOR EXAMPLE THAT, TEACHES THE PRIOR ART, YOU DON'T NEED
7 TO CITE ALL OF THEM.

8 Q. YOU DON'T NEED TO CITE ALL OF THEM?

9 A. THAT'S MY UNDERSTANDING.

10 Q. AND YOU'VE CITED TO THE PATENT AND TRADEMARK OFFICE SOME
11 PRIOR ART?

12 A. WELL, THE SAIKI PAPER FOR EXAMPLE.

13 Q. THE SAIKI PAPER, WHAT IS THAT?

14 A. IT WAS A PAPER PUBLISHED -- WAS REALLY THE FIRST PAPER FROM
15 CETUS, I THINK, THAT DESCRIBED THIS PROCESS WHICH THEY CALLED
16 POLYMERASE CHAIN REACTION, WAS PUBLISHED IN SCIENCE IN 1985.

17 Q. AND DO YOU -- DO YOU HAVE AN OPINION AS TO WHETHER THE
18 TEACHINGS OF THE SAIKI PAPER ARE MORE SIGNIFICANT OR LESS
19 SIGNIFICANT THAN THE KHORANA PRIOR ART, ABOUT THE SAME?

20 A. ABOUT THE SAME. AS I'VE SAID, SAIKI PAPER DESCRIBED THE
21 PRINCIPLE OF TWO PRIMERS ON A TEMPLATE IN SEQUENTIAL ROUNDS OF
22 PRIMER EXTENSION, AS DID THE KHORANA PRIMER.

23 Q. YOU TOLD MR. PASAHOV I BELIEVE THAT YOU'VE NOT DONE A PCR
24 REACTION WITH YOUR OWN HANDS?

25 A. THAT'S CORRECT.

WALLACE-REDIRECT/FIGG

8 1 Q. PLEASE DESCRIBE YOUR INVOLVEMENT WITH THE RUNNING OF PCR
2 REACTIONS IN YOUR LABORATORIES BY THE PEOPLE WHO ARE EMPLOYED BY
3 YOU?

4 A. WELL, MY OFFICE IS ABOUT JUST A SHORT DISTANCE FROM MY
5 LABORATORY AND I'M CONSTANTLY IN THE LABORATORY. I INTERACT
6 WITH PEOPLE, THEY SHOW ME THEIR RESULTS.

7 IN THE CASE OF A PCR EXPERIMENT WE'LL DISCUSS IT. DID
8 IT WORK? DID IT NOT WORK? DID IT WORK POORLY? AND WE WILL PUT
9 OUR HEADS TOGETHER AND COME UP WITH A SERIES OF EXPERIMENTS TO
10 TRY TO IMPROVE THINGS OR TO ACHIEVE THE GOALS OF THE EXPERIMENT,
11 THAT'S THE MOST IMPORTANT THING. SO IT'S UPON MY
12 RECOMMENDATIONS THAT MANY OF THE CONDITIONS GET CHANGED AND
13 SUCCESS CAN BE ACHIEVED.

14 Q. NOW, WHEN DO YOU RECALL FIRST READING THE KLEPPE PAPER AND
15 THE PANET PAPER?

16 A. AS I SAID, I DON'T TOTALLY RECALL. IT WAS LAST YEAR
17 SOMETIME.

18 Q. SOMETIME WHEN I BROUGHT IT TO YOUR ATTENTION?

19 A. YES.

20 Q. MR. PASAHOW WAS ASKING YOU ABOUT YOUR REFERENCES TO SOME
21 KHORANA PAPERS IN THE REVIEW ARTICLE YOU WROTE IN 1984, DO YOU
22 RECALL THAT?

23 A. YES, I DO RECALL THAT.

24 Q. DO YOU KNOW HOW MANY PAPERS DR. KHORANA'S LAB HAS PUBLISHED?

25 A. NO, I DOESN'T KNOW, BUT IT'S MANY.

WALLACE-REDIRECT/FIGG

1 Q. TEN?

2 A. HUNDREDS.

3 Q. THREE OR FOUR HUNDRED?

4 A. PROBABLY.

5 Q. DID YOU STUDY ALL OF THOSE THREE OR FOUR HUNDRED ARTICLES OR
6 HOWEVER MANY IT WAS, WHEN YOU WERE A GRADUATE STUDENT?

7 A. NO, I DID NOT.

8 Q. DO YOU HAVE ANY RECOLLECTION THAT YOU EVER SAW THE KLEPPE
9 PAPER, PANET PAPER OR DR. KHORANA'S NSF GRANT APPLICATION BEFORE
10 I SHOWED THEM TO YOU LAST YEAR?

11 A. I HAVE NO RECOLLECTION.

12 Q. NOW, MR. PASAHOW REFERRED TO SOME STATEMENTS THAT YOU HAVE
13 MADE IN SOME OF YOUR PUBLISH ARTICLES. IN PARTICULAR HE POINTED
14 YOU TO A STATEMENT IN EXHIBIT B-151, IN WHICH YOU POINTED OUT
15 THAT PCR IMPROVES THE SENSITIVITY OF THE PROBING REACTION AND
16 YOU CITED THE SAIKI PAPER, DO YOU RECALL THAT TESTIMONY?

17 A. I DO.

18 Q. THIS MAYBE REDUNDANT, BUT DO YOU BELIEVE YOU KNEW OF THE
19 PANET PAPER, OR THE KLEPPE PAPER, OR THE NSF GRANT APPLICATION
20 WHEN YOU ATTRIBUTED THAT STATEMENT TO THE SAIKI PAPER?

21 A. WHEN I WROTE THIS PAPER I DON'T RECALL HAVING READ THOSE
22 OTHER PAPERS, NO.

23 Q. NOW, SINCE I CALLED THE KLEPPE PAPER AND PANET PAPERS TO
24 YOUR ATTENTION LAST YEAR, HAVE YOU WRITTEN ANY OTHER ARTICLES
25 ABOUT -- THAT DEAL WITH PCR?

WALLACE-REDIRECT/FIGG

1 A. YES, I HAVE.

2 Q. HAVE THOSE BEEN PUBLISHED YET?

3 A. ONE PAPER IS IN PRESS.

4 Q. HAVE YOU CITED THE KLEPPE PAPER, OR THE PANET PAPER, OR
5 OTHER PRIOR ART OF DR. KHORANA'S IN CONNECTION WITH THE PCR
6 REACTION IN ANY OF YOUR SUBSEQUENT PAPERS?

7 A. YES, I REFER TO THE KLEPPE PAPER AS A REFERENCE FOR THE
8 SEQUENTIAL ROUNDS OF PRIMER EXTENSION PROCESS KNOWN AS PCR. I
9 FEEL IT'S ONLY FAIR AS A SCIENTIST TO GIVE HIM CREDIT FOR HAVING
10 SAID THAT. THEM CREDIT.

11 Q. DR. WALLACE, WHEN YOU USE THIS WORD "PCR" IN YOUR
12 PUBLICATIONS, CAN YOU DESCRIBE TO THE JURY WHAT THAT DENOTES,
13 WHAT THAT MEANS WHEN YOU USE THE TERM IN THE MODERN DAY SENSE?

14 A. WELL, I THINK I TRIED TO EXPLAIN IT EARLIER. PCR IS A --
15 YOU'VE SEEN ME MOVING THESE PIECES ON THIS EXHIBIT, BUT PCR IS
16 REALLY A PROCESS WHERE YOU PUT A REACTION IN A TUBE, PUT IT IN A
17 MACHINE AND GO AWAY AND COME BACK AND THEN DO SOME EXPERIMENTS.

18 ITS GOTTEN TO THE STAGE WHERE BECAUSE OF DEVELOPMENTS
19 SUCH AS THE THERMOSTABLE ENZYME AND THE AUTOMATED INSTRUMENTS
20 THAT IT'S DONE WITHOUT THE TECHNICIAN REALLY GETTING TOO
21 INVOLVED WITH THE STEPS OF DENATURATION, ADDING ENZYME, ET
22 CETERA. YOU REALLY ONLY HAVE TO ADD ENZYME ONCE AND
23 DENATURATION -- CURES BY AUTOMATIC MACHINE.

24 Q. IN THIS PAPER THAT MR. PASAHOW REFERRED YOU TO YOU ACTUALLY
25 SITE TWO SAIKI PAPERS, ONE PUBLISHED IN 1985 AND ONE PUBLISHED

WALLACE-REDIRECT/FIGG

9 1 IN 1988, DO YOU SEE THAT, B-151?

2 A. YES.

3 Q. WHEN YOU USED THE WORD PCR IN THAT PAPER, ARE YOU REFERRING
4 TO THE TWO OR THREE CYCLE AMPLIFICATION PROCESS OF THE CLAIM OR
5 ARE YOU REFERRING TO THE MODERN DAY UNDERSTANDING WHAT PCR IS?

6 A. IT'S THE MODERN DAY UNDERSTANDING.

7 Q. MR. PASAHOW SORT OF CRITICIZED DOCTORS. ROSSI AND ITAKURA
8 FOR NOT REFERRING TO THE KLEPPE OR THE PANET PAPERS, DO YOU
9 RECALL DR. ITAKURA OR DR. ROSSI EVER TELLING YOU THEY KNEW OF
10 THE KLEPPE OR THE PANET PAPERS?

11 A. NO, I DON'T RECALL THEM TELLING ME THAT.

12 Q. HAVE YOU DISCUSSED THOSE PAPERS WITH THEM RECENTLY?

13 A. I MAY HAVE DISCUSSED WITH DR. ROSSI, I HAVEN'T SEEN DR.
14 ITAKURA THAT MUCH.

15 Q. THAT DR. ROSSI INDICATED TO YOU HE KNEW OF THE KLEPPE PAPER
16 A LONG TIME AGO.

17 MR. PASAHOW: EXCUSE ME, YOUR HONOR, THAT QUESTION
18 OBVIOUSLY CALLS FOR HEARSAY.

19 THE COURT: OBJECTION SUSTAINED.

20 MR. FIGG: IF I MAY, YOUR HONOR, IT'S NOT NECESSARILY
21 HEARSAY. I MEAN, DOCTOR -- MR. PASAHOW WAS INQUIRING OR
22 IMPLYING DR. ROSSI KNEW OF THAT AND DIDN'T CITE IT. WHAT WE'RE
23 REALLY INQUIRING INTO IS WHAT WAS THE STATE OF DR. ROSSI'S
24 KNOWLEDGE.

25 THE COURT: I THINK YOU'RE GOING TO HAVE TO CALL DR.

WALLACE-REDIRECT/FIGG

10 1 ROSSI, OTHERWISE ONE MAY READ ABOUT A PAPER DOCUMENT AND
2 DETERMINE WHAT'S THERE OR NOT, BUT WHAT WAS IN SOMEONE ELSE'S
3 MIND OR WHAT THEY MAY HAVE SAID OUT OF COURT IS HEARSAY.

4 THE OBJECTION IS SUSTAINED.

5 Q. (BY MR. FIGG) DO YOU RECALL MR. PASAHOW PUTTING UP ON THE
6 THE TV SCREEN THE LITTLE DIAGRAMS OF THE EXPERIMENT THAT DR.
7 ROSSI WAS DOING?

8 A. YES, I DO.

9 Q. YOU MADE A COMMENT IT WOULDN'T MAKE SENSE FOR DR. ROSSI TO
10 HAVE DONE PCR AT THAT POINT, CAN YOU ELABORATE ON WHAT YOU MEANT
11 BY THAT?

12 A. WELL, WHAT DR. ROSSI WAS REALLY TRYING TO DO WAS BUILD A
13 GENE AND THROUGH THE YEARS THE WAY GENES WERE ASSEMBLED WAS TO
14 BUILD THE BUILDING BLOCKS AND THEN PUT IT TOGETHER WITH AN
15 ENZYME, WHICH I DESCRIBED TO YOU EARLIER, SO THAT IN ORDER TO
16 SYNTHESIZE A GENE OF A PARTICULAR LENGTH YOU HAD TO ESSENTIALLY
17 SYNTHESIZE ALL THE NUCLEOTIDES FOR BOTH STRANDS WHICH WAS A
18 SIGNIFICANT AMOUNT OF WORK.

19 WHAT DR. ROSSI AND DOCTOR ITAKURA TOGETHER HAD DECIDED
20 WOULD BE PRACTICAL WAS TO SYNTHESIZE THE GENE AND ESSENTIALLY
21 TWO PIECES OR IN THIS CASE FOUR PIECES, BUT WHERE THE TWO PIECES
22 OVERLAPPED AT THEIR ENDS, SO YOU'VE SYNTHESIZED ONE STRAND
23 PARTWAY AND THE OTHER STRAND PARTWAY, BUT YOU HAVEN'T
24 SYNTHESIZED ALL OF THE NECESSARY NUCLEOTIDES OF THE WHOLE GENE.

25 AND THEN SIMPLY BY ADDING DNA POLYMERASE IT WILL PRIMER

WALLACE-REDIRECT/FIGG

10 1 EXTEND THOSE MOLECULES TO COMPLETE THE DOUBLE STRAND. SO YOU'VE
2 USED AN ENZYME TO FINISH THE JOB THAT IT HAD TAKEN SEQUENCING TO
3 DO EARLIER.

4 HE HAPPENED TO DO THIS PARTICULAR EXPERIMENT IN TWO
5 PIECES THEN PUT THOSE PIECES TOGETHER BY LIGASE, BUT THAT WAS
6 THE PRINCIPLE BEHIND WHAT HE WAS TRYING TO DO.

7 Q. MR. PASAHOW AGAIN RAISED THE ISSUE OF PRIMER EXTENSION
8 REACTION AS USED IN SEQUENCING REACTIONS. AGAIN, PERHAPS AT THE
9 RISK OF BEING REDUNDANT, CAN YOU EXPLAIN WHY THE PRIMER
10 EXTENSION REACTION DOESN'T ALWAYS GO TO THE END WHEN ONE IS
11 TRYING TO DETERMINE THE SEQUENCE OF A PIECE OF DNA?

12 A. FIRST OF ALL, PRIMER EXTENSIONS WERE UNDERSTOOD BEFORE
13 DOCTOR SANGER STARTED HAD TO USE THIS AS A METHOD OF SEQUENCING.
14 THE IDEA WAS TO USE A SPECIFIC PRIMER WHICH WOULD BIND TO A
15 SPECIFIC SITE ON THE MOLECULE TO BE SEQUENCED.

16 THE ENZYME DNA POLYMERASE WOULD EXTEND THE PRIMER
17 THROUGH A REGION OF UNKNOWN SEQUENCE AND BY DOING SO IT WOULD BE
18 COPYING INFORMATION OF THAT ELEMENT OF UNKNOWN SEQUENCE. BY
19 INTRODUCING SPEAK REAGENTS WITH SPECIFIC BUILDING BLOCKS WHICH
20 STOP IN ONE REACTION.

21 FOR EXAMPLE AT C'S AND ANOTHER REACTION AT T'S AND
22 ANOTHER REACTION AT A'S AND SO ON, YOU WILL HAVE EXTENDED THE
23 MOLECULE UNTIL IT GETS TO A PARTICULAR A.

24 NOW, THAT ONLY HAPPENS IN ONE SAY, FOR EXAMPLE, IN ONE
25 PARTICULAR PRIMER EXTENSION, BUT IN ANOTHER ONE IT MAY GO TO THE

WALLACE-REDIRECT/FIGG

10 1 NEXT A, AND TO THE NEXT A. AND THEN BY ORDERING THESE FRAGMENTS
2 PRODUCED BY THIS PRIMER EXTENSION REACTION IN WHAT'S CALLED AN
3 ALANOVEL (PHONETIC) YOU CAN USE TO SEPARATE THEM ON THE BASIS OF
4 LENGTH, YOU CAN SEE WHERE EVERY A IS, EVERY T IS, EVERY G. IT'S
5 NECESSARY FOR THAT REACTION TO WORK PROPERLY YOU NEED TO BE
6 CONDUCTING VERY SPECIFIC PRIMER EXTENSION FROM A SPECIFIC
7 STARTING POINT.

11 8 Q. IT'S NOT BY ACCIDENT THAT THEY'RE NOT GOING ALL THE WAY TO
9 THE END OR IT'S NOT A SHORTCOMING OF THE PRIMER EXTENSION
10 REACTION, IS THAT YOUR TESTIMONY?

11 A. THAT'S CORRECT. IT WAS UNDERSTOOD AND KNOWN THAT IF YOU
12 DIDN'T HAVE THESE REAGENTS WHICH STOPPED THE PRIMER EXTENSION
13 FROM GOING TO THE END, THAT THE PRIMER EXTENSIONS WOULD
14 CONTINUE.

15 IN FACT, MR. HONG'S FIRST STRAND SYNTHESIS AS WE
16 DISCUSSED EARLIER ACTUALLY TOOK ADVANTAGE OF THAT THE PRIMER
17 EXTENSION STARTED AT A SPECIFIC SPOT AND EXTENDED THROUGH A
18 REGION OF UNKNOWN SEQUENCE PIECED THE REGION OF UNKNOWN SEQUENCE
19 TO A REGION OF KNOWN SEQUENCE.

20 Q. MR. PASAHOV SORT OF CRITICIZED YOU FOR NOT CITING THE HONG
21 PAPERS AND YOUR OWN PAPER -- SEQUENCING DOUBLE STRANDED DNA TO
22 THE PATENT OFFICE. AGAIN, WHAT PRIOR ART DID YOU CITE TO THE
23 PATENT OFFICE IN CONNECTION WITH YOUR OWN PATENT APPLICATIONS?

24 A. THE SAIKI REFERENCE, I WOULD BELIEVE.

25 Q. DOES THE SAIKI REFERENCE TEACH ANYTHING ABOUT CONDUCTING A

WALLACE-REDIRECT/FIGG

11 1 PRIMER EXTENSION ERECTION ON DOUBLE STRANDED DNA?

2 A. THAT'S THE WHOLE POINT OF THE SAIKI PAPER, IS PRIMER
3 EXTENSION ON TWO PRIMERS ON DOUBLE STRANDED DNA TEMPLATE TO
4 PERFORM THE MULTIPLE CYCLES TO AMPLIFY A PIECE OF DNA.

5 Q. SO DO YOU HAVE ANY CONCLUSION OR OPINION AS TO WHETHER THE
6 HONG PAPERS ARE MORE PERTINENT THAN SAIKI PAPERS THAT YOU DID
7 CITE TO THE PATENT OFFICE?

8 A. WELL, THEY'RE NOT MORE PERTINENT. THE SAIKI PAPER
9 DEMONSTRATED THE DOUBLE STRANDED DNA COULD SERVE AS A TEMPLATE
10 FOR PRIMER EXTENSIONS, AS DID THE HONG PAPER.

11 THE COURT: MR. FIGG, IT'S GOING ON 1:15.

12 MR. FIGG: WE PROBABLY HAVE A LITTLE MORE, YOUR HONOR,
13 MAYBE 15, 20 MINUTES.

14 THE COURT: AND THEN WHERE DOES THAT LEAVE US WITH YOU,
15 MR. PASAHOW?

16 MR. PASAHOW: I HAVE ABOUT ONE MINUTE SO FAR, YOUR
17 HONOR. I CAN'T IMAGINE IT WOULD GO ON FOR MORE THAN FIVE.

18 THE COURT: I'VE LIKE TO FINISH UP WITH DR. WALLACE SO
19 HE DOESN'T HAVE TO COME BACK, SO WE CAN START A NEW WITNESS
20 TOMORROW. IF WE CAN MOVE THINGS ALONG.

21 MR. FIGG: I'LL TRY TO MOVE IT ALONG, YOUR HONOR.

22 THE COURT: IF YOU CAN. A NUMBER OF QUESTIONS HAVE
23 ALREADY BEEN ANSWERED, HE'S ANSWERED THAT IN HIS TESTIMONY LET'S
24 NOT HAVE A REITERATION WHAT WAS STATED ALREADY.

25 Q. (BY MR. FIGG) WE WERE TALKING ABOUT THE HONG PAPERS, DR.

WALLACE-REDIRECT/FIGG

11 1 WALLACE, AND I REFERRING TO EXHIBIT 109, I BELIEVE YOUR -- THE
2 REFERENCE TO YOUR ARTICLE IS REFERENCE SIX IN THAT PAPER; IS
3 THAT CORRECT?

4 A. WELL, I BELIEVE SO. I DON'T HAVE IT IN FRONT OF ME. WE
5 WENT OVER THAT. YES, REFERENCE SIX.

6 MR. FIGG: NATURALLY WHEN YOU TELL ME TO SPEED IT UP I
7 CAN'T FIND THE EXHIBIT, I APOLOGIZE.

8 THE COURT: HE HAS IT UP HERE.

9 Q. (BY MR. FIGG) REFERRING TO THE FIRST PAGE OF THE HONG
10 ARTICLE, DR. WALLACE, EXHIBIT 109, WHAT DOES DR. HONG SAY WITH
11 RESPECT TO YOUR METHOD OF SEQUENCING DOUBLE STRANDED DNA ON
12 SMALL DOUBLE STRANDED DNA MOLECULES?

13 ONE OF THE PROBLEMS I BELIEVE IS THAT THE COPY YOU HAVE
14 IS ILLEGIBLE, YOU MAY ACTUALLY WANT TO REFER TO THE POSTER.

15 A. WELL, IT SAYS IT'S REFERRING TO OUR METHOD THAT WE HAVE
16 SHOWN THAT IT IS POSSIBLE TO SEQUENCE SMALL DOUBLE STRANDED DNA
17 MOLECULES. SO IT'S REFERRING TO THE SUCCESS OF THE EXPERIMENTS
18 PUBLISHED IN THESE THREE REFERENCES.

19 Q. WHAT KIND OF DNA MOLECULE WAS DR. HONG TRYING TO SEQUENCE?

20 A. HE WAS USING A MOLECULE WHICH WAS LARGE, THAT'S A RELATIVE
21 TERM, BUT I'D SAY APPROXIMATELY TEN TIMES LARGER THAN THE
22 MOLECULES WE WERE USING IN THESE EXPERIMENTS.

23 Q. IN FACT, IT WAS 48,000 OF THESE BUILDING BLOCKS?

24 A. OF THESE BUILDING BLOCKS.

25 Q. WAS DR. HONG -- FROM YOUR READING OF THE PAPER, WAS DR. HONG

WALLACE-REDIRECT/FIGG

11 1 SUCCESSFUL IN OBTAINING SEQUENCE INFORMATION FROM THAT LONG
2 MOLECULE?

3 A. YES, HE WAS.

4 Q. NOW, YOU DIDN'T WORK WITH MOLECULES THAT LONG IN YOUR
5 SEQUENCING PAPER; IS THAT RIGHT?

6 A. NO, I DID NOT.

7 Q. WHAT WERE THE SIZE OF THE MOLECULES YOU WERE WORKING WITH,
8 ROUGHLY?

9 A. ABOUT 5,000 APPROXIMATELY BUILDING BLOCKS.

10 Q. NOW, REFERRING BACK TO THE PROCESS DESCRIBED IN CLAIM 1 OF
11 THE '202 PATENT, HOW LONG ARE THE MOLECULES THERE THAT THE
12 PRIMER EXTENSION REACTION IS BEING CONDUCTED ON?

13 A. THAT'S SUCH A BROAD CLAIM, THEY COULD BE AS SMALL AS YOU
14 WANTED THEM TO BE REALLY EXCEPT THAT PRIMERS WOULD HAVE TO BE
15 ABLE TO PRIME ON THEM. SO VERY SMALL MOLECULES OF 25 LONG WOULD
16 WORK, ACCORDING TO THE CLAIM.

17 Q. COULD THEY BE MUCH -- WELL, I TAKE IT FROM THAT THEY COULD
18 BE MUCH SMALLER THAN THE SMALL MOLECULES WITH WHICH YOU
19 SUCCESSFULLY USED PRIMER EXTENSION IN DOUBLE STRANDING DNA
20 SEQUENCING?

21 A. YES, MUCH SMALLER. MR. PASAHOW ASKED YOU SOME QUESTIONS
22 ABOUT THE RATIOS OF PRIMERS TO THE TEMPLATES IN THE KLEPPE
23 PAPER, DO YOU RECALL THAT?

24 A. YES, I DO.

25 Q. NOW, THE LAST PARAGRAPH OF THE KLEPPE PAPER THERE IS SOME

WALLACE-REDIRECT/FIGG

12 1 ADVISE ABOUT WHAT RATIO OF PRIMER TO TEMPLATE SHOULD BE USED, DO
2 YOU RECALL THAT?

3 A. YES, I DO.

4 Q. WHAT DOES IT SAY ABOUT THAT?

5 A. I DON'T KNOW THE EXACT LANGUAGE. IT SAYS THE DENATURATION
6 STEP WOULD BE CARRIED OUT IN THE PRESENCE OF SUFFICIENTLY LARGE
7 EXCESS OF THE TWO APPROPRIATE PRIMERS.

8 Q. DO YOU HAVE AN OPINION AS TO WHETHER THIS REFERENCE TO A
9 LARGE EXCESS OF THE TWO APPROPRIATE PRIMERS HERE REFERS TO THE
10 RATIOS OF ONE TO ONE AND TWO TO ONE THAT MR. PASAHOW WAS
11 DIRECTING YOUR ATTENTION TO IN THE BODY OF THE PAPER?

12 A. NO, I THINK IT REFERS TO THE FACT THAT HE'S GOING TO DO AN
13 AMPLIFICATION REACTION AND NEEDS AN EXCESS IN ORDER TO ACHIEVE
14 AMPLIFICATION. AS I SAID, EACH ROUND CONSUMES PRIMER, SO HE'S
15 SAYING THAT YOU NEED TO ADD AN EXCESS.

16 Q. MR. PASAHOW ALSO ASKED YOU ABOUT THE RATIOS OF PRIMERS TO
17 TEMPLATES IN THE PANET PAPER, DO YOU RECALL THAT?

18 A. YES.

19 Q. TRY TO GET THE POSTER OF THAT ONE HERE, TOO.

20 JUST TO SPEED THINGS ALONG. DO YOU RECALL THAT IN THE
21 REFERENCE TO DOCTOR MOLINEUX' WORK IN THE PANET PAPER, IT
22 DIRECTED THE USE OF TEN TIMES OR MORE PRIMERS?

23 A. THAT'S WHAT I SAID, YES.

24 Q. ACTUALLY IT SAID -- WHEN DID IT SAY TO ADD THOSE PRIMERS?

25 A. IT SAYS . . . IT SAYS THAT YOU NEEDED THE PRIMERS TO BE

WALLACE-REDIRECT/FIGG

12 1 PRESENT IN EXCESS OF TEN TIMES OR MORE. AND THEN IT GOES ON TO
2 SAY, IT IS FURTHER NECESSARY TO ADD AFTER EACH CYCLE FRESH
3 AMOUNTS OF PRIMERS SO AS TO MAINTAIN THE PROPER PRIMER TEMPLATE
4 RATIOS.

5 Q. WHAT DO YOU UNDERSTAND PROPER PRIMER TEMPLATE RATIOS TO MEAN
6 THERE?

7 A. TEN TIMES OR MORE EXCESS. AN EXCESS.

8 Q. SO IF YOU FOLLOWED THE TEACHINGS OF THAT PAPER AND CONDUCTED
9 MULTIPLE CYCLES OF AMPLIFICATION, LET'S SAY, YOU PERFORMED TEN
10 CYCLES OF AMPLIFICATION, HOW MANY PRIMERS WOULD YOU HAVE
11 RELATIVE TO THE AMOUNT OF DNA THAT YOU STARTED WITH?

12 A. THEY SAID 1,000 WOULD CONSUME APPROXIMATELY 1,000 PRIMERS
13 FOR EVERY MOLECULE THAT WAS BEING AMPLIFIED.

14 Q. AND YOU WOULD HAVE MUCH MORE THAN A TEN TO ONE RATIO AT THE
15 END OF THAT SERIES OF CYCLES, WOULDN'T YOU?

16 A. THAT'S CORRECT. IF YOU ADDED TEN TIMES IN THE FIRST ROUND
17 YOU ONLY CONSUME ONE, YOU HAVE NINE THE NEXT TIME YOU HAVE TO
18 ADD AN EXCESS AND ONLY ONE, TWO WOULD GET CONSUMED AND SO ON, SO
19 AT THE END OF YOU HAVE AN EXCESS.

20 Q. NOW, THIS SEQUENCING REACTION IS NOT AN AMPLIFICATION
21 PROCEDURE; IS THAT RIGHT?

22 A. THAT'S CORRECT.

23 Q. AND SEQUENCING -- DOES SEQUENCING INVOLVE MULTIPLE CYCLES OF
24 HEATING AND COOLING?

25 A. NO, NOT NORMALLY.

WALLACE-REDIRECT/FIGG

12 1 Q. SO DO YOU NEED THE LARGE EXCESS OF PRIMERS IN THE SEQUENCING
2 REACTION THAT YOU NEED IF YOU'RE GOING TO RUN MULTIPLE CYCLES OF
3 AN AMPLIFICATION REACTION?

4 A. NO, YOU DON'T NEED THEM. IN FACT, PROBABLY A DETRIMENT.

5 Q. WOULD A PERSON OF ORDINARY SKILL IN 1984 RECOGNIZED THE
6 DIFFERENCE BETWEEN THOSE TWO KIND OF REACTIONS?

7 A. IN MY OPINION, IT WOULD.

8 Q. WHY WOULD A SCIENTISTS IN 1984 FOLLOWING THE TEACHINGS OF
9 DR. KHORANA'S PUBLICATIONS HAVE SELECTED A DIFFERENT ENZYME THAN
10 THE ONE DR. KHORANA USED?

11 JUST TO RECAP, I BELIEVE YOU SAID DR. KHORANA USED DNA
12 POLYMERASE 1 AND THIS PERSON IN 1984 WOULD HAVE BEEN LIKELY TO
13 CHOOSE THE KLENOW FRAGMENT?

14 A. BASED ON YOUR EXPERIENCE AND THE EXPERIENCE OF OTHERS IN
15 USING ENZYMES. SEQUENCING REACTIONS, FOR EXAMPLE, OFTEN USE THE
16 KLENOW FRAGMENT OF DNA POLYMERASE. PROBABLY WOULD HAVE SAID
17 WELL, DOCTOR KLEPPE AND DR. KHORANA'S LAB WERE USING DNA
18 POLYMERASE WITH ONE THAT WAS AVAILABLE TO THEM, BUT TODAY I
19 WOULD DO THESE EXPERIMENTS WITH KLENOW DNA POLYMERASE.

20 Q. WOULD THE ORDINARY SKILLED SCIENTISTS IN 1984 HAVE KNOWN
21 THAT KLENOW WOULD HAVE SOME ADVANTAGES OVER THE ENZYME THAT DR.
22 KHORANA USED BACK IN 1972?

23 A. YES, THEY UNDERSTOOD THE BIOCHEMISTRY OF THE -- THE
24 BIOCHEMICAL DIFFERENCE BETWEEN THE TWO ENZYMES.

25 MR. FIGG: I THINK WE'LL STOP THERE, YOUR HONOR.

WALLACE-RE CROSS/PASAHOW

13 1 THANK YOU, DR. WALLACE.

2 THE COURT: STILL ONE QUESTION?

3 MR. PASAHOW: I BELIEVE SO, YOUR HONOR.

4 RE CROSS-EXAMINATION

5 BY MR. PASAHOW:

6 Q. DR. WALLACE, LET ME SHOW YOU WHAT I'VE MARKED AS EXHIBIT
7 B-203, CAN YOU CONFIRM FOR ME THAT WAS THE PATENT OFFICE'S
8 RESPONSE AFTER YOU FILED THE AMENDMENT THAT MR. FIGG MARKED
9 DURING YOUR REDIRECT EXAM?

10 A. I GUESS IT WAS THE PATENT OFFICE RESPONSE, YES.

11 MR. PASAHOW: YOUR HONOR, THE ONLY REMAINING THING, I
12 WOULD OFFER A SERIES OF EXHIBITS. THE FIRST IS B-168 WHICH IS
13 THE PATENT APPLICATION SERIAL NUMBER 402,450; B-187 WHICH IS THE
14 APPLICATION NUMBER 143,05; B-188 WHICH IS THE APPLICATION NUMBER
15 187,428; B-189 WHICH IS THE APPLICATION 283,142; B-190 WHICH WAS
16 THE ARTICLE BY DR. ITAKURA ET AL. SYNTHESIS AND USE OF
17 OLIGONUCLEOTIDES; B-192 WHICH WAS THE MOLECULAR BIOLOGY OF HOMO
18 SAPIENS, COLD SPRING, MASS. SYMPOSIUM VOLUME; AND B-203 WHICH IS
19 THE OFFICE ACTION IN PATENT APPLICATION NUMBER 143,045 THAT I
20 JUST MARKED.

21 MR. FIGG: WE HAVE NO OBJECTION TO THOSE, YOUR HONOR.
22 I BELIEVE MANY OF THEM COME IN UNDER SEAL UNDER THAT PROTECTIVE
23 ORDER, HOWEVER.

24 THE COURT: THAT IS CORRECT. REFERS TO THE PATENT
25 APPLICATIONS. ARE THERE ANY OTHER DOCUMENTS WITHIN THAT GROUP

WALLACE-RECCROSS/PASAHOW

13 1 THAT COME WITHIN THAT CATEGORY?

2 MR. PASAHOW: NO, YOUR HONOR.

3 MR. FIGG: WELL, THE PROSECUTION DOCUMENTS, I BELIEVE.

4 MR. PASAHOW: ONE EACH OF US FILED.

5 MR. FIGG: IN THAT REGARD WE WOULD -- WE MARKED A-170
6 AND WE MOVE THE ADMISSION OF THAT. THAT'S THE AMENDMENT THAT
7 WAS FILED.

8 MR. PASAHOW: THERE'S NO OBJECTION.

9 THE COURT: THAT AGAIN IS ANOTHER ONE THAT'S SEALED.

10 MR. FIGG: YES.

11 THE COURT: WHAT OTHER ONE BESIDES THE FIRST THREE THAT
12 HAVE TO BE SEALED AND THE ONE MR. FIGG JUST REFERRED TO SO IT'S
13 CLEAR ON THE RECORD.

14 MR. PASAHOW: THE ONES THAT WOULD NEED TO BE SEALED ARE
15 B-168 THROUGH B-189.

16 THE COURT: THOSE ARE THE APPLICATIONS.

17 MR. PASAHOW: YES, AND B-203.

18 THE COURT: AND ALL OF THOSE ARE SEALED.

19 WHAT THAT MEANS, LADIES AND GENTLEMEN, IS THAT MEMBER
20 OF THE PUBLIC GOING THROUGH THE CLERK'S OFFICE TO TRY TO SEE THE
21 RECORDS IN THIS CASE HAS ACCESS TO PAPERS THAT ARE FILED.
22 THERE'S SOME ITEMS THAT BECAUSE OF THEIR NATURE IT'S NOT
23 APPROPRIATE TO DO SO.

24 OF COURSE, THEY WILL BE AVAILABLE TO YOU FOR YOUR
25 EVALUATION AND CONSIDERATION OF THE CASE DURING DELIBERATIONS.

WALLACE-RE CROSS/PASAHOW

13 1 BUT AGAIN NOT TO BE DISCUSSED OUTSIDE OF THESE PROCEEDINGS AND
2 IN YOUR DELIBERATIONS.

3 ANYTHING FURTHER?

4 MR. FIGG: NO, YOUR HONOR.

5 MR. PASAHOW: NO, YOUR HONOR. THANK YOU FOR YOUR
6 PATIENCE WITH US.

7 THE COURT: OKAY. THAT DR. WALLACE, YOU ARE EXCUSED.
8 THANK YOU.

9 (WITNESS EXCUSED)

10 THE COURT: AND, LADIES AND GENTLEMEN, SO ARE YOU.
11 THANK YOU FOR BEING PATIENT AND WAITING, BUT THAT WAY WE FINISH
12 DR. WALLACE'S TESTIMONY AND WE WILL START WITH ANOTHER WITNESS
13 TOMORROW. AND WE'LL SEE YOU TOMORROW AND FOLLOW THE
14 INSTRUCTIONS I'VE GIVEN YOU. SEE YOU TOMORROW AT 8:00 O'CLOCK.

15 THE COURT: ANYTHING ELSE WE NEED TO TAKE UP NOW,
16 COUNSEL?

17 MR. PASAHOW: APPARENTLY NOT, YOUR HONOR, WE'RE STILL
18 TRYING TO AGREE ON THE INSTRUCTION WHICH WILL RESOLVE THE ISSUE
19 OF LAW ABOUT THE OVERLAPPING CIRCLES.

20 MR. FIGG: THE ONLY OTHER THING --

21 THE COURT: BY THAT TIME THEY WILL HAVE FORGOT IT.

22 MR. FIGG: I'M AFRAID THAT MAY ALREADY WITH THE CASE.
23 WE'VE ALSO TRANSMITED TO YOUR HONOR THROUGH MS. MORIYAMA A
24 PROPOSED ORDER, SORT OF PUTTING THE CASE ON ICE UNTIL WE GET
25 FINISHED WITH THIS ONE. I DON'T KNOW IF YOU'VE SEEN THAT ONE OR

WALLACE-RE CROSS/PASAHOW

1 NOT.

2 THE COURT: OKAY. YES. IT WAS HANDED UP BY JUST -- I
3 JUST SAW THE TITLE ON IT. IT WAS ANOTHER PIECE OF PAPER I
4 DIDN'T REALIZE IT WAS AN ORDER.

5 MR. PASAHOW: I THINK, YOUR HONOR, IT ACCURATELY
6 REFLECTS THE COURT'S RULING ON THIS.

7 THE COURT: AND THE ORDER RELATING CASES HAS ALREADY
8 BEEN SIGNED.

9 MR. PASAHOW: I HAVE NOT SEEN THAT.

10 MR. FIGG: WE HAVEN'T SEEN IT.

11 THE CLERK: DID YOU FILE A NOTICE OF RELATED CASE?

12 MR. FIGG: THEY DID.

13 THE COURT: OFF THE RECORD.

14
15 (THE ABOVE MATTER ADJOURNED AT 1:35 P.M.)
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