

# The Road Taken

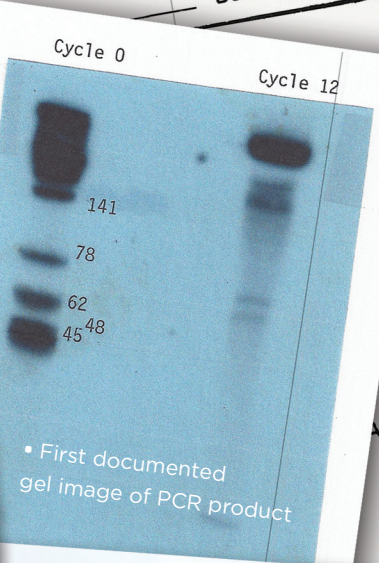
Celebrating 30 Years of PCR

1

**The Birth of PCR:**  
From the lab notebook of Kary Mullis  
September 8, 1983

Project No. \_\_\_\_\_  
Book No. \_\_\_\_\_

129



chain reaction #01  
primers 10 µM  
KM23  
A 489 picomolar  
4 µl/µL  
dNTPs 0.5 mM  
DNA pol I Klenow 25 units  
PIES buffer

Butler Deluxe 1/2.5  
about:  
250 mM Tris  
250 mM PIPES  
pH 6.8 with NaOH  
20 mM MgCl<sub>2</sub>  
0.5 mM BSA  
0.25 mM DTT

Highway 128 at mile marker 46.58; the road of inspiration where Kary Mullis conceived of PCR  
Photo: Nancy Cosgrove Mullis

Photo: Nancy Cosgrove Mullis

begin 12:00 midnight 9-8  
Put in the same place:  
10 µL 0.1 mM KM23  
10 µL 0.1 mM KM23  
5 µL each 10 mM dNTPs  
20 µL hum DNA 1 µL/µL  
5 µL Klenow @ 5U/µL  
40 µL Butler Deluxe  
+ PIPES = Piperazine-N,N'-bis[2-ethanesulfonic acid]  
allow that the DNA and KM23 be brought to 100° together 2' and quick cooled.  
To Page No. \_\_\_\_\_  
Date 9-8-83  
Invented by Kary Mullis  
Recorded by \_\_\_\_\_  
Witnessed & Understood by me, \_\_\_\_\_  
Date \_\_\_\_\_

"...innovation is also on its face often marked with a bit of insanity. If no one mentions loudly that one thinks you're out of your mind, then, you probably are not being innovative." - Kary Mullis

ATCC GCC CTG ACG  
CTA ACA GTCC



2

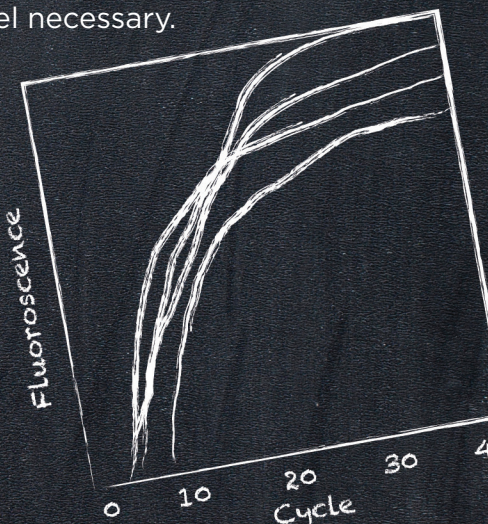
**Multiplex PCR:**  
Multiple targets can be detected from one reaction—1988.

3

**Real-time PCR:**  
Measures the reaction as it proceeds. No gel necessary.

4

**Digital PCR:**  
Sample dilution & distribution into independent reactions allows absolute quantification and rare allele detection



5

**BHQ® dye technology:**  
A true dark quencher for qPCR is introduced.

## Clinical Lab Request - Genetics

(PLEASE WRITE THE NUMBER ON THE SAMPLE BAG)

Sample ID No. \_\_\_\_\_ Subsamples A- \_\_\_\_\_

Lab Number: \_\_\_\_\_

SAMPLE IDENTIFICATION: Official ☐ Unofficial ☐

Commodity: \_\_\_\_\_ Lot Number: \_\_\_\_\_

Variety: \_\_\_\_\_ Origin: \_\_\_\_\_

Company: \_\_\_\_\_ Contact: \_\_\_\_\_

Address: \_\_\_\_\_ City: \_\_\_\_\_

State: \_\_\_\_\_ Phone/Fax: \_\_\_\_\_

Reason for sample: \_\_\_\_\_

Alitalia ☐ ALK FISH ☐ BRAF Mutations ☐ EGFR Mutations ☐ IDH Mutations ☐ KRAS Mutations ☐ Mutations, AML ☐ Mutations, Melanoma ☐ VEGFR Mutations, GIST ☐ VEGFR Mutations, DNA Test

Status as of 09:00 GMT

Pandemic (H1N1) virus

Number of laboratory confirmed cases as reported to WHO

Map produced 01 July 2009 11:38 GMT

FAM-TGC AGT CCT CGC TCA CTG GGC ACG-BHQ

7 FAM-BHQ probes used to monitor H1N1 pandemic

Food Safety Turns to Real-time PCR

Real-time PCR assays also developed for food safety testing, such as screening for E. Coli

Personalized Cancer Gene Diagnostic Assays

BRCA1  
BRCA2  
CDH1  
STK11  
TP53

PCR-based tests revolutionize oncology healthcare, allowing medical professionals to make better, informed clinical decisions

8

9

10

1980

1990

2000

2010

2020

9

**Point-of-Care (POC)**  
genetic testing expedites diagnosis and treatment

10

From a legacy of DNA synthesis to the future of PCR, Biosearch empowers inventors and visionaries

19% / 72%

87%

29% 78%

27%

29% 78%

87%

19% / 72%

27%

**BIOSEARCH TECHNOLOGIES**  
Advancing Nucleic Acid Technology™

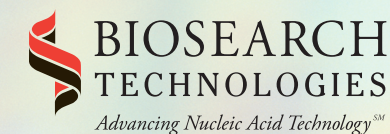


## MOLECULAR INSIGHT, AMPLIFIED.

It takes sophisticated tools to reveal the secrets of biology. So when quality can't be compromised, scientists turn to Biosearch Technologies to synthesize the exact oligonucleotides they need. At our new world-class facilities, we build our products as if lives depend on it, because they often do. Our proprietary BHQ® probes enable reliable qPCR testing for the most consequential applications – whether that's detection of cancer cells, genetic mutations, wine-spoiling microbes, or bio-threat agents. And that's just today. Who knows what we'll help you discover tomorrow?



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### About Biosearch Technologies:

The roots of Biosearch Technologies can be traced back to 1978 when President and CEO, Ron Cook, PhD founded "Biosearch, Inc." to supply research tools to the nascent biotechnology industry. In the 1980s, Biosearch developed and manufactured automated, solid-phase DNA synthesizers, including the SAM I as shown to the right. These instruments manufactured oligonucleotides with prodigious proficiency, catalyzing the development of revolutionary oligonucleotide-based technologies. Most notably in 1982, Kary Mullis at Cetus Corporation used a SAM I DNA synthesizer to create oligos for use in his experiments, which eventually resulted in the invention of the Polymerase Chain Reaction process (PCR).



The invention of PCR forever changed the molecular biology world. An enabling technology, it is a standard and indispensable research technique used for numerous medical and biological applications such as DNA sequencing and genetic fingerprinting. PCR was also the lone technique that helped the synthetic oligonucleotide business become a thriving industry. Hence, 30 years later, Biosearch respectfully commemorates the development of a technique that swiftly answered previous DNA chemistry problems with, as Kary Mullis describes, "Abundance and distinction."

The original Biosearch was sold, and Ron Cook founded Biosearch Technologies, Inc. (Biosearch) in 1993. Since that time, Biosearch has become an acknowledged leader in the design, development, and manufacture of sophisticated oligonucleotide-based tools for real-time, quantitative PCR, Stellaris® RNA FISH, and other nucleic acid-based applications. The unique properties of Biosearch's Black Hole Quencher® (BHQ®) dyes have led to their ubiquitous use in dual-labeled qPCR probes worldwide.

Biosearch Technologies is an ideal partner for assay and medical device development because Biosearch can supply businesses at all stages of product development from design through commercialization. A vertically integrated structure allows Biosearch precise control over raw materials and manufacturing processes, reducing costs and turnaround time for the benefit of Biosearch customers. Biosearch's manufacturing processes also conform to GMP requirements per 21 CFR Part 820, when applicable.

Biosearch products currently enable the human diagnostic, ag/bio, veterinary diagnostic, food safety, pharmaceutical, public health and biodefense industries, and have been used as components in a long list of regulated medical devices.

To learn more about Biosearch Technologies, visit our website: [www.biosearchtech.com](http://www.biosearchtech.com).

# PCR

Past,  
Present,  
& Future

*The Road Taken: Celebrating 30 Years of PCR*