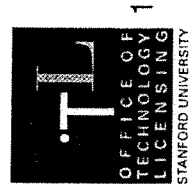


Stanford University
Office of Technology Licensing

Stanford wishes to offer a license
to its invention entitled:

**“PCR Assays for Monitoring
Antiviral Therapy and Making
Therapeutic Decisions in the
Treatment of AIDS”**

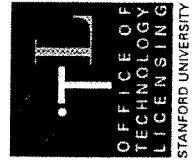


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Outline

- Why is Stanford Interested in Licensing This Technology to Roche?
- Background of Technology
- What is Stanford Offering?
- The Offer
- Next Steps

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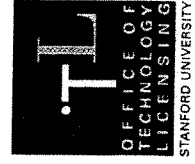
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Why Roche?

- Stanford and Roche have had a long and fruitful relationship
- Although other companies might have an interest, we believe that Roche would be the best partner for Stanford for the subject Stanford IP

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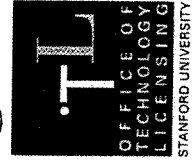


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Background of Technology

- During the early 1990's, Dr. Mark Holodniy working under Dr. Merigan with support from Dr. Katzenstein studied DNA in cells for a possible diagnostic of HIV
- Cetus Scientists were working on DNA as a diagnostic test
- Refer to UCSF/Cetus article 'Risk of HIV-1 in Screened Blood Donations' The New Eng. J. of Medicine, Vol. 325, No. 1 Pp. 1-5

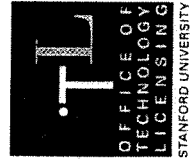


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STAN 029346

Background of Technology

- Meanwhile at Stanford, studies were being conducted on RNA in plasma for a possible diagnostic and quantification of HIV following therapy
- Refer to Stanford/Cetus article ‘Detection and Quantification of HIV RNA in Patient Serum by Use of PCR,’ in The Journal of Infectious Diseases, April 1991 Pp. 862-866

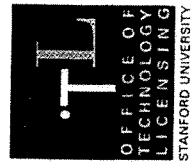


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Background of Technology

- Refer to Stanford article “Reduction in Plasma Human Immunodeficiency Virus Ribonucleic Acid after Dideoxynucleoside Therapy as Determined by PCR”, JCI 88:1755-1759, 1991

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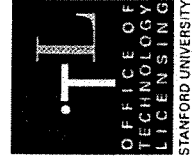
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Background of Technology

- The value of quantification of HIV RNA in plasma serum was not evident to Cetus at that time or through June 1992
- Refer to ‘Detection of Human Retroviruses by PCR,’ in Annals of Medicine, June 1992 Pp. 211-214
- Cetus subsequently explored detection of proviral DNA in PBMCs and various tissues

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Background of Technology

- However, Dr. Holodniy, Dr. Katzenstein and Dr. Merigan had conceived that measurement of HIV RNA from plasma could be used for assessing efficacy of antiviral therapy
- Refer to Stanford article “Reduction in Plasma Human Immunodeficiency Virus Ribonucleic Acid after Dideoxynucleoside Therapy as Determined by PCR”, JCI 88:1755-1759, 1991

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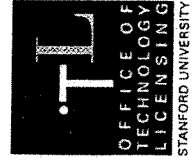


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Background of Technology

- Follow on work at Stanford showed that the test could be ultra-sensitive. This presented an opportunity to provide a test that could be used by every patient to monitor therapy
- Refer to Stanford article "Biological Variation and Quality Control of Plasma RNA Quantitation by RT PCR" JCM, vol. 31:2960-2966, 1993

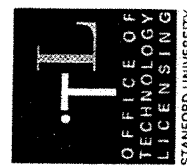


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Background of Technology

- Dr. Merigan's, Dr. Katzenstein's and Dr. Holodniy's work resulted in the issuance of U.S. Patent No. 5,968,730, among others
- Continuations based on the same application "family" remain pending

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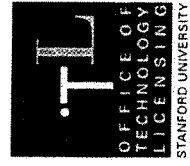
What are we offering? Stanford's IP:

• A method for evaluating the effectiveness of anti-HIV therapy of a patient:

- collecting a plasma sample from an HIV-infected patient who is being treated with an antiretroviral agent;
- amplifying the HIV-encoding nucleic acid in the plasma sample using HIV primers in about 30 cycles of PCR; and
- testing for the presence of HIV-encoding nucleic acid, in the product of the PCR;

in which the absence of detectable HIV-encoding nucleic acid correlates positively with the conclusion that the antiretroviral agent is therapeutically

effective. See U.S. Patent No. 5,968,730, Claim 1



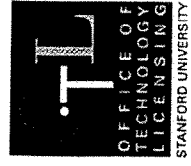
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Stanford's IP (cont.)

- Collecting a plasma sample from an HIV-infected patient who is being treated with an antiretroviral agent
- quantification of viral load in human plasma
- assessment of patient prognosis
- monitoring of effect of concurrent antiretroviral therapy
- useful in clinical management of HIV infected patients

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Stanford's IP (cont.)

- Amplifying the HIV-encoding nucleic acid in the plasma sample using HIV primers in about 30 cycles of PCR
- PCR assay of plasma HIV RNA
- Use of HIV primers about 20-30 bases long

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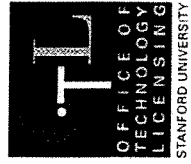


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Stanford's IP (cont.)

- Testing for the presence of HIV-encoding nucleic acid, in the product of the PCR
 - quantification of nucleic acid by hybridizing product of PCR with detectably labeled probe that is complementary to the HIV sequence
 - amount of signal generated by probe hybridized to PCR product can be compared to amount of signal generated by probe hybridized to a known copy number of HIV, e.g., by using a microwell plate reader

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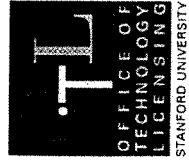


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Stanford's IP (cont.)

- The absence of detectable HIV-encoding nucleic acid correlates positively with the conclusion that the antiretroviral agent is therapeutically effective
- decreased nucleic acid copy number correlates with effective therapy
- increased nucleic acid copy number correlates with disease progression

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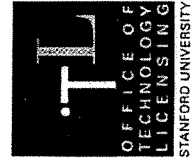
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The Offer

- Stanford wishes to extend to Roche an offer to obtain an Exclusive License to the subject Stanford IP
- License would include rights to patents that may issue based on pending applications from same patent “family”
- Stanford inventors Drs. Merigan, Holodniy and Katzenstein would be available to collaborate with Roche Scientists

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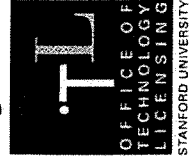


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The Offer (cont.)

- The license will contain other terms and conditions normally found in Stanford's licenses and reasonably acceptable to Roche
- The offer extended hereunder is valid until May 31, 2000, unless withdrawn prior to that date
- No license or other rights are implied by this document



Next Steps

- Terms and conditions would be negotiated in good faith within 90 days of Stanford's receipt of Roche's written acceptance
- We look forward to continuing our relationship through a mutually acceptable license agreement to this technology

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