BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
John E. Tavis	Professor
eRA COMMONS USER NAME Tavisje	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Minnesota - Morris	B.A.	1981-1985	Biology and Chemistry
Pennsylvania State University	Ph.D.	1985-1990	Molec. and Cell. Biology
Pennsylvania State University	Post-Doc	1990-1991	Molec. and Cell. Biology
University of California – San Francisco	Post-Doc	1991-1994	Molecular Virology

A. PERSONAL STATEMENT:

My lab has 2 research programs whose goals are to reduce suffering from viral hepatitis. The first project is to explore the biochemistry and cell biology of the reverse transcriptase from the Hepatitis B Virus. This project has been ongoing for 15 years. The second project is to evaluate the effect of Hepatitis C Virus' very high genetic diversity on its response to antiviral therapy and on disease induced by HCV infection. The HCV project has been ongoing since 2001. The translational aspects of this research that began following my service on the Steering Committee for the Virahep-C clinical trial for HCV have yielded patent applications for both the HBV and HCV projects. I am also active in the international virology community, having organized the 2003 International Meeting on the Molecular Biology of HBV, served on the American Society for Virology program committee, chaired an American Cancer Society study section, served as a reviewer for many journals, and have recently been appointed to 3 national service positions: An academic editor for *PLoS One*, a permanent member of the VirB NIH study section, and a member of the American Cancer Society Council for Extramural Research. This experience has given me a broad perspective on virology.

B. POSITIONS and HONORS:

1994 - 2002 Assistant Professor, Department of Molecular Microbiology & Immunology
Saint Louis University Health Sciences Center
2002 - 2007 Associate Professor, Department of Molecular Microbiology & Immunology
Saint Louis University Health Sciences Center
2007 – present Professor, Department of Molecular Microbiology & Immunology
Saint Louis University Health Sciences Center

1985 - 1988 NSF Graduate Fellow
2001 - 2008 NIDDK Virahep-C clinical study steering committee
2002 Tenure at Saint Louis University
2003 Co-organizer for the International Meeting on the Molecular Biology of the Hepatitis B Viruses
2003 - 2005 American Society for Virology program committee
2003 - 2006 American Cancer Society molecular and cell biology of cancer (MBC) peer review group (Vice-Chair 2005, Chair 2006)
2008 – present Study section *ad hoc* service: **ACS**: MBC (01/08), Site visit team (09/08); **NIH**: CE (06/08), VirB (02/09), BST-S (03/09), ZRG1 IDM-C (05/09 and 07/09), ZRG1 OBT-A (05/09), ACE (03/10), VirB (06/10).
2009 – present American Cancer Society, Eastern Missouri region community ambassador.
2009 – present Academic Editor, *PLoS One.*
2010 - 2016 NIH VirB study section, permanent member.
2010 – present Saint Louis University Cancer Center Internal Advisory Committee.
2011 - 2015 American Cancer Society Council on Extramural Grants.
2011 University of Minnesota – Morris Distinguished Alumnus Award.

2007 US Patent 12/144,030 (Pending), *Sequence Covariance Networks, Methods and Uses Therefor*. Aurora, R., Donlin, M.J., and **Tavis, J.E.**

2010 Provisional US Patent 61/428,543 (Pending). *Network Threading Approach for Predicting a Patient's Response to Hepatitis C Virus Therapy*. Aurora R. and **Tavis, J.E.**

2011 Provisional US Patent 61/481,949 (Pending). *A generalized Network Threading Approach for Predicting a Patient's Response to Hepatitis C Virus Therapy*. Aurora R. and **Tavis, J.E.**

C. PUBLICATIONS:

1. **Tavis, J.E.**, Walker, D.L., Gardner, S.D., and Frisque, R.J. (1989). Nucleotide sequence of the human polyomavirus AS, an antigenic variant of BK virus. *J. Virol.* **63**:901-911. PMCID: PMC247764.
2. **Tavis, J.E.**, Frisque, R.J., Walker, D.L., and White III, F.A. (1990). Antigenic and transforming properties of the DB strain of the human polyomavirus BK virus. *Virology* **178**:568-572.
3. **Tavis, J.E.** and Frisque, R.J. (1991). Altered DNA binding and replication activities of JC virus T-antigen mutants. *Virology* **183**:239-250.
4. **Tavis, J.E.** and Ganem, D. (1993). Expression of functional hepatitis B virus polymerase in yeast reveals it to be the sole viral protein required for correct initiation of reverse transcription. *Proc. Natl. Acad. Sci. USA* **90**:4107-4111. PMCID: PMC46455.
5. **Tavis, J.E.**, Trowbridge, P.W., and Frisque, R.J. (1994). Converting the JCV T antigen RB binding domain to that of SV40 does not alter JCV's limited transforming activity but does eliminate viral viability. *Virology* **199**:384-392.
6. **Tavis, J.E.**, Perri, S., and Ganem, D. (1994). Hepadnaviral reverse transcription initiates within the stem-loop of the packaging signal and employs a novel strand transfer. *J. Virol.* **68**:3536-3543. PMCID: PMC236857.
7. Ganem, D., Pollack, J.R., and **Tavis, J.E.** (1994). Hepatitis B virus reverse transcriptase and its many roles in hepadnaviral genomic replication. *Infect. Agents Dis.* **3**:85-93.
8. **Tavis, J.E.** and Ganem, D. (1995). RNA sequences controlling the initiation and transfer of duck hepatitis B virus minus-strand DNA. *J. Virol.* **69**:4283-4291. PMCID: PMC189167.
9. Gerelsaikhan, T., **Tavis, J.E.**, and Bruss, V. (1996). Envelopment of hepatitis B virus nucleocapsids does not occur in the absence of DNA replication. *J. Virol.* **70**:4269-4274. PMCID: PMC190358.
10. **Tavis, J.E.** and Ganem, D. (1996). Evidence for activation of the hepatitis B virus polymerase by binding of its RNA template. *J. Virol.* **70**:5741-5750. PMCID: PMC190587.
11. Wei, Y., **Tavis, J.E.**, and Ganem, D. (1996). Relationship between viral DNA synthesis and virion envelopment in hepatitis B viruses. *J. Virol.* **70**:6455-6458. PMCID: PMC190679.
12. **Tavis, J.E.** (1996). The replication strategy of the hepadnaviruses. *Viral Hep. Rev.* **2:**205-218.
13. **Tavis, J.E.**, Massey, B., and Gong, Y. (1998). The duck hepatitis B virus polymerase is activated by its RNA packaging signal, γ. *J. Virol.* **72**:5789-5796. PMCID: PMC110380.
14. Gong, Y., Yao, E., Stevens, M., and **Tavis, J.E.** (2000). Evidence that the first strand transfer of duck hepatitis B virus reverse transcription requires the polymerase and that strand transfer is not needed for the switch of the polymerase to the elongation mode of DNA synthesis. *J. Gen. Virol.* **81**:2059-2065.
15. Yao, E., Gong, Y., Chen, N., and **Tavis, J.E.** (2000). The majority of the duck hepatitis B virus reverse transcriptase in cells is non-encapsidated and is bound to a cytoplasmic structure. *J. Virol.* **74**:8648-8657. PMCID: PMC116376.
16. Gong, Y., Yao, E., and **Tavis, J.E.** (2001). Evidence that the RNAseH activity of the duck hepatitis B virus is unable to act on exogenous substrates. *BMC Microbiology* **1**:12. PMCID: PMC37354.
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18. Yao, E. and **Tavis, J.E.** (2003). Kinetics of synthesis and turnover of the duck hepatitis B virus reverse transcriptase. *J. Biol. Chem.* **278:**1201-1205.
19. Yao, E., Schaller, H., and **Tavis, J.E.** (2003). The duck hepatitis B virus polymerase and core proteins accumulate in different patterns from their common mRNA. *Virology* **311:**81-88.

20. Yao, E. and **Tavis, J.E.** (2003). Localization of duck hepatitis B virus polymerase within cells. Chapter 27 in *Methods in Molecular Medicine: Hepatitis B and D Protocols*, R. Hamatake and J. Lau, eds., Humana Press, Totawa, New Jersey.
21. **Tavis, J.E.**, Cao, F., and Yao, E. (2003). Metabolism of the hepadnaviral reverse transcriptase. *Recent Res. Devel. Virol*. **5:**83-96.
22. Sen, N., Cao, F., and **Tavis, J.E.** (2004). Translation of the duck hepatitis B virus reverse transcriptase by ribosomal shunting. *J. Virol.* **78:**11751-11757. PMCID: PMC523253.
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29. Badtke, M.P., Cao, F., and **Tavis, J.E.** (2006). Combining genetic and biochemical approaches to identify functional molecular contact points. *Biol. Proced. Online* **8:**77-86. PMCID: PMC1592461.
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31. Zhang, Z. and **Tavis, J.E.** (2006). The duck hepatitis B virus reverse transcriptase functions as a full-length monomer. *J. Biol. Chem.* **281:**35794-35801.
32. Zhou, D., Fan,X, Tan, D., Xu, Y., **Tavis, J.E.**, and Di Bisceglie, A.M. (2007). Separation of near full-length hepatitis C virus quasispecies variants from a complex population. *J. Virol. Meth.* **141:**220-224.
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34. Donlin M.J., Cannon, N.A., Yao, E., Li, J., Wahed, A., Taylor, M.W., Belle, S.H., Di Bisceglie, A.M., Aurora, R., and **Tavis, J.E.** for the Virahep-C Study Group. (2007). Pretreatment sequence diversity differences in the full-length hepatitis C virus coding region correlates with early response to therapy. *J. Virol.* **81:**8211–8224. PMCID: PMC1951276.
35. Brodsky, L.I., Wahed, A., Li, J., **Tavis, J.E.**, Tsukahara, T., and Taylor, M.W. (2007). A novel unsupervised method to identify genes important in the anti-viral response: Application to interferon/ribavirin in hepatitis C patients. *PLoSOne* **1:**e584. PMCID: PMC1978073.
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37. Cannon, N.A., Donlin, M..J., Fan, X., Aurora, R., and **Tavis, J.E.** for the Virahep-C Study Group. (2008). Hepatitis C virus diversity and evolution in the full open-reading frame during antiviral therapy. *PloS One* **3:**e2123. PMCID: PMC2373758.
38. Aurora, R., Donlin, M.J., Cannon, N.A., and **Tavis, J.E.** for the Virahep-C Study Group. (2009). Genome-wide hepatitis C virus amino acid covariance networks can predict response to antiviral therapy in humans. *J. Clin. Invest*. **119:**225-236. PMCID: PMC2613460.
    Commentary: Oh, T.S. and Rice, C.M. (2009). Predicting response to hepatitis C therapy. *J. Clin Invest.* **119:**5-7.

Research Highlight: Basson, M. (2009). Heads up on HCV. Nature Medicine **15:**148.

39. Cao, F., Scougall, C.A., Jilbert, A.R., and **Tavis, J.E.** (2009). "Pre-P" is a secreted glycoprotein encoded as an N-terminal extension of the duck hepatitis B virus polymerase gene. *J. Virol.* **83:**1368-1378. PMCID: PMC2620893.
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45. Donlin, M.J., Cannon, N.A., Aurora, R., Li, J., Wahed, A.S., Di Bisceglie, A.M., and **Tavis, J.E.** for the Virahep-C Study Group. (2010). Contribution of genome-wide HCV genetic differences to outcome of interferon-based therapy in Caucasian American and African American patients. *PLoS One* **5:**e9032. PMCID: PMC2815788.
46. Wagoner, J., Negash, A., Kane, O.J., Martinez, L.E., Nahmias, Y., Bourne, N., Owen, D.M., Grove, J., Brimacombe, C., McKeating, J.A., Pécheur E.-I., Graf, T.N., Oberlies, N.H., Lohmann, V., Cao F., **Tavis, J.E.**, and Polyak. S.J. (2010). Multiple effects of silymarin on the Hepatitis C virus lifecycle. *Hepatology* **51:**581-592.
47. **Tavis, J.E.**, Donlin, M.J., Aurora, R., Fan, X., and Di Bisceglie, A.M. (2011). Prospects for personalizing antiviral therapy for HCV with pharmacogenetics. *Genome Medicine* **3:**8.
48. Wagoner, J., Morishima, C., Graf, T.N., Oberlies, N.H., Teissier, E., Pécheur, E.I., **Tavis, J.E.**, and Polyak, S.J. (2011). Differential in vitro effects of intravenous versus oral formulations of silibinin on the HCV life cycle and inflammation. *Plos One* **6:**e16464. PMCID: PMC3030583.
49. Cao, F., Donlin, M.J., Turner, K., Cheng, X., and **Tavis, J.E.** (2011). Genetic and biochemical diversity in the HCV NS5B RNA polymerase in the context of interferon α plus ribavirin therapy. *J. Viral Hep.* **18:**349-357. PMCID: In Process.
50. Cao, F. and **Tavis, J.E.** (2011). RNA Elements needed for translation of the Duck Hepatitis B Virus polymerase via ribosomal shunting. *J. Virol.* **85:**6343-6352. PMCID: In Process.

D. RESEARCH SUPPORT:

ONGOING

No number yet (Tavis, P.I.) 08/01/11 – 07/31/12 DATES NOT CONFIRMED
Saint Louis University President's Research Fund Award
Biochemical characterization of the HBV RNAseH as a novel drug target

The major goal of this institutional seed grant is to perform a basic biochemical characterization of recombinant Hepatitis B virus RNAseH proteins from divergent HBV genotypes in preparation for drug screening.

U54 AI057160 (Virgin, P.I.) 03/01/09 – 02/28/14
NIH/NIAID
Midwest Regional Center of Excellence for Biodefense

Dr. Tavis is a HCV viral genetics expert for this multi-center grant (2% effort; no lab support).

R01 CA126807 (Tavis, P.I.) 01/14/08 - 12/31/12
NIH/NCI
HCV genetic variation and hepatocellular carcinoma
The major goal of this project is to determine how natural sequence variation in the full-length HCV genome affects its oncogenic potential through a combination of genetic and functional analyses.

R01 DK080711 (Fan, P.I.) 03/01/08 – 02/28/12
NIH/NIDDK
Hepatitis C Virus Quasispecies in the Resistance to Antiviral Therapy
The major goal of this application is to evaluate patterns of genetic variation in the full-length HCV quasispecies during antiviral therapy.

R01 DK074515 (Tavis, P.I.) 07/15/07 – 06/30/12
NIH/NIDDK
Role of HCV sequence variation in pathology
The major goal of this project is to determine how natural sequence variation in the full-length HCV genome affect its virulence in collaboration with the HALT-C clinical study (In no-cost extension).

R43 GM088948 (Zhang, P.I.) 08/01/10 – 01/31/12
NIH/NIGM
Direct RT-PCR detection of RNA pathogens and mRNA expression in crude samples
The major goal of this project is to determine whether PCR additives and specialized Taq polymerases produced by DNA Polymerase Technology, Inc. permit robust direct RT-PCR amplification RNAs from serum or plasma. Dr. Tavis is P.I. of a subcontract from DNA Polymerase Technology to perform the testing of surplus patient samples.

<u>RECENTLY COMPLETED</u>

2-30013 (Tavis, P.I.) 02/01/10 – 02/28/11
Saint Louis University President's Research Fund Award
HCV covariance networks as biomarkers of non-response to therapy
The major goal of this institutional seed grant was to obtain HCV sequence information for viruses infecting 12 patients for whom the outcome of interferon-based therapy is known. This is being used to guide development of sequence-based algorithms to predict the outcome of therapy.

R43 AI84232 (Cao, P.I.) 08/01/09 – 07/31/10
NIH/NIAID
An HBV polymerase RNA binding assay suitable for inhibitor screening
The major goal of this project is to identify the form of recombinant HBV reverse transcriptase best suited for use in a screen for therapeutic inhibitors of RNA binding by the enzyme. Dr. Tavis relinquished the role of P.I. on this project to Dr. Cao when the NIAID converted the application from an R41 STTR to an R43 SBIR grant.

R01 AI057573 (Morrison, P.I.) 05/01/04 - 01/30/10
NIH/NIAID
Functional analysis of HSV2 tegument proteins in mice
The major goal of this project was to examine the function and contribution to pathogenesis of the HSV2 tegument proteins UL13 and VP22 in cultured cells and in mice.

R21 CA125321 (Tavis, P.I.) 06/07/07 – 05/31/09
NIH/NCI
Variation in NTP use by the HCV polymerase and response to therapy
The major goal of this project was to determine how natural variation in the HCV RNA polymerase affects its use of ribavirin triphosphate.

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R01 AI38447 (Tavis, P.I.) 07/01/96 - 04/30/08
NIH/NIAID
Analysis of the hepadnaviral reverse transcriptase

The major goal of this project was to obtain a molecular understanding of the hepatitis B virus reverse transcriptase, using the duck hepatitis B virus enzyme as a model. We studied the activity of the enzyme, its structure, and its interaction with cells.

R03 AI059050 (Morrison, P.I.) 03/01/05 – 02/28/08
NIH/NIAID
Substrate recognition motif of the HSV-2 UL13 kinase

The major goal of this project was to identify the substrate recognition motif of the HSV-2 UL13 protein kinase to guide subsequent efforts to determine the role of UL13 in viral replication and pathology.

No Project Number (Tavis, P.I.) 09/01/05 – 08/31/07
Friends of the St. Louis University Liver Center
Mechanism of ribavirin action through the HCV NS5B RNA polymerase

The goal of this project was to determine if natural variation in the HCV NS5B RNA-dependent RNA polymerase modulates incorporation of the antiviral nucleoside analog ribavirin, hence modulating its effectiveness.

U01 DK60345 (Tavis, P.I.) 07/01/01 - 04/30/07
NIH/NIDDK
Response of HCV to therapy in African Americans

The major goal of this project was to analyze genetic variation in HCV associated with success or failure of antiviral therapy with pegylated interferon alpha plus ribavirin in African Americans and Caucasian Americans.