



Universiteit
Leiden
The Netherlands

Zebrafish embryos and Larvae : a new generation of disease model and drug screens

Ali, S.

Citation

Ali, S. (2011, December 7). *Zebrafish embryos and Larvae : a new generation of disease model and drug screens*. Retrieved from <https://hdl.handle.net/1887/18191>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/18191>

Note: To cite this publication please use the final published version (if applicable).

References

1. Dahm R, Geisler R (2006) Learning from small fry: the zebrafish as a genetic model organism for aquaculture fish species. *Mar Biotechnol (NY)* 8: 329-345.
2. Van den Belt K, Van PS, Witters H (2000) Toxicity of cadmium-contaminated clay to the zebrafish *Danio rerio*. *Arch Environ Contam Toxicol* 38: 191-196.
3. Shin JT, Fishman MC (2002) From Zebrafish to human: modular medical models. *Annu Rev Genomics Hum Genet* 3: 311-340.
4. Rubinstein AL (2003) Zebrafish: from disease modeling to drug discovery. *Curr Opin Drug Discov Devel* 6: 218-223.
5. Goldsmith P (2004) Zebrafish as a pharmacological tool: the how, why and when. *Curr Opin Pharmacol* 4: 504-512.
6. Hill AJ, Teraoka H, Heideman W, Peterson RE (2005) Zebrafish as a model vertebrate for investigating chemical toxicity. *Toxicol Sci* 86: 6-19.
7. Zon LI, Peterson RT (2005) In vivo drug discovery in the zebrafish. *Nat Rev Drug Discov* 4: 35-44.
8. Reimers MJ, La Du JK, Periera CB, Giovanini J, Tanguay RL (2006) Ethanol-dependent toxicity in zebrafish is partially attenuated by antioxidants. *Neurotoxicol Teratol* 28: 497-508.
9. Parg C, Roy NM, Ton C, Lin Y, McGrath P (2007) Neurotoxicity assessment using zebrafish. *J Pharmacol Toxicol Methods* 55: 103-112.
10. Kari G, Rodeck U, Dicker AP (2007) Zebrafish: an emerging model system for human disease and drug discovery. *Clin Pharmacol Ther* 82: 70-80.
11. Lieschke GJ, Currie PD (2007) Animal models of human disease: zebrafish swim into view. *Nat Rev Genet* 8: 353-367.
12. Barros TP, Alderton WK, Reynolds HM, Roach AG, Berghmans S (2008) Zebrafish: an emerging technology for in vivo pharmacological assessment to identify potential safety liabilities in early drug discovery. *Br J Pharmacol* 154: 1400-1413.
13. Brittijn SA, Duivesteijn SJ, Belmamoune M, Bertens LF, Bitter W, de Bruijn JD, Champagne DL, Cuppen E, Flik G, Vandenbroucke-Grauls CM, Janssen RA, de Jong IM, de Kloet ER, Kros A, Meijer AH, Metz JR, van der Sar AM, Schaaf MJ, Schulte-Merker S, Spaink HP, Tak PP, Verbeek FJ, Vervoordeldonk MJ, Vonk FJ, Witte F, Yuan H, Richardson MK (2009) Zebrafish development and regeneration: new tools for biomedical research. *Int J Dev Biol* 53: 835-850.
14. Tsang M (2010) Zebrafish: A tool for chemical screens. *Birth Defects Res C Embryo Today* 90: 185-192.

15. Bull J, Levin B (2000) Perspectives: microbiology. Mice are not furry petri dishes. *Science* 287: 1409-1410.
16. Barnes DM (1986) Tight money squeezes out animal models. *Science* 232: 309-311.
17. Verkman AS (2004) Drug discovery in academia. *Am J Physiol Cell Physiol* 286: C465-C474.
18. Redfern WS, Waldron G, Winter MJ, Butler P, Holbrook M, Wallis R, Valentin JP (2008) Zebrafish assays as early safety pharmacology screens: paradigm shift or red herring? *J Pharmacol Toxicol Methods* 58: 110-117.
19. Berghmans S, Butler P, Goldsmith P, Waldron G, Gardner I, Golder Z, Richards FM, Kimber G, Roach A, Alderton W, Fleming A (2008) Zebrafish based assays for the assessment of cardiac, visual and gut function--potential safety screens for early drug discovery. *J Pharmacol Toxicol Methods* 58: 59-68.
20. Flinn L, Bretaud S, Lo C, Ingham PW, Bandmann O (2008) Zebrafish as a new animal model for movement disorders. *J Neurochem* 106: 1991-1997.
21. Tanguay RL, Reimers MJ (2008) Analysis of ethanol developmental toxicity in zebrafish. *Methods Mol Biol* 447: 63-74.
22. Best JD, Berghmans S, Hunt JJ, Clarke SC, Fleming A, Goldsmith P, Roach AG (2008) Non-associative learning in larval zebrafish. *Neuropsychopharmacology* 33: 1206-1215.
23. Grunwald DJ, Eisen JS (2002) Headwaters of the zebrafish -- emergence of a new model vertebrate. *Nat Rev Genet* 3: 717-724.
24. Gerlai R, Lahav M, Guo S, Rosenthal A (2000) Drinks like a fish: zebra fish (*Danio rerio*) as a behavior genetic model to study alcohol effects. *Pharmacol Biochem Behav* 67: 773-782.
25. Gerlai R (2003) Zebra fish: an uncharted behavior genetic model. *Behav Genet* 33: 461-468.
26. Nei M, Xu P, Glazko G (2001) Estimation of divergence times from multiprotein sequences for a few mammalian species and several distantly related organisms. *Proc Natl Acad Sci U S A* 98: 2497-2502.
27. Kimmel CB, Ballard WW, Kimmel SR, Ullmann B, Schilling TF (1995) Stages of embryonic development of the zebrafish. *Dev Dyn* 203: 253-310.
28. Falk-Petersen IB (2005) Comparative organ differentiation during early life stages of marine fish. *Fish Shellfish Immunol* 19: 397-412.
29. Nüsslein-Volhard (2002) The morphology of larval and adult zebrafish. In: Nüsslein-Volhard C, Dahm R, editors. *Zebrafish: A practical approach*. Tubingen: Oxford university press. pp. 59-94.
30. Westerfield M (2000) *The Zebrafish Book. A Guide for the Laboratory Use of Zebrafish (Danio rerio)*. 4th Edition :

31. Wielhouwer EM, Ali S, Al-Afandi A, Blom MT, Olde Riekerink MB, Poelma C, Westerweel J, Oonk J, Vrouwe EX, Buesink W, Vanmil HG, Chicken J, van 't OR, Richardson MK (2011) Zebrafish embryo development in a microfluidic flow-through system. *Lab Chip* 11: 1815-1824.
32. Ali S, Champagne DL, Alia A, Richardson MK (2011) Large-scale analysis of acute ethanol exposure in zebrafish development: a critical time window and resilience. *PLoS ONE* 6: e20037.
33. Macphail RC, Brooks J, Hunter DL, Padnos B, Irons TD, Padilla S (2009) Locomotion in larval zebrafish: Influence of time of day, lighting and ethanol. *Neurotoxicology* 30: 52-58.
34. Irons TD, Macphail RC, Hunter DL, Padilla S (2010) Acute neuroactive drug exposures alter locomotor activity in larval zebrafish. *Neurotoxicol Teratol* 32: 84-90.
35. Ali S, van Mil HG, Richardson MK (2011) Large-scale assessment of the zebrafish embryo as a possible predictive model in toxicity testing. *PLoS ONE* 6: e21076.
36. Fraysse B, Mons R, Garric J (2006) Development of a zebrafish 4-day embryo-larval bioassay to assess toxicity of chemicals. *Ecotoxicol Environ Saf* 63: 253-267.
37. Organisation for Economic Cooperation and Development (1998) OECD Guideline For Testing of Chemicals. OECD 212. Fish, Short-term Toxicity Test on Embryo and Sac-Fry Stages.
38. Gerlai R, Lahav M, Guo S, Rosenthal A (2000) Drinks like a fish: zebra fish (*Danio rerio*) as a behavior genetic model to study alcohol effects. *Pharmacol Biochem Behav* 67: 773-782.
39. Fernandes Y, Gerlai R (2009) Long-Term Behavioral Changes in Response to Early Developmental Exposure to Ethanol in Zebrafish. *Alcohol Clin Exp Res*
40. Yang L, Ho NY, Alshut R, Legradi J, Weiss C, Reischl M, Mikut R, Liebel U, Muller F, Strahle U (2009) Zebrafish embryos as models for embryotoxic and teratological effects of chemicals. *Reprod Toxicol* 28: 245-253.
41. Lockwood B, Bjerke S, Kobayashi K, Guo S (2004) Acute effects of alcohol on larval zebrafish: a genetic system for large-scale screening. *Pharmacol Biochem Behav* 77: 647-654.
42. Dlugos CA, Rabin RA (2003) Ethanol effects on three strains of zebrafish: model system for genetic investigations. *Pharmacol Biochem Behav* 74: 471-480.
43. Dlugos CA, Rabin RA (2007) Ocular deficits associated with alcohol exposure during zebrafish development. *J Comp Neurol* 502: 497-506.
44. Berghmans S, Butler P, Goldsmith P, Waldron G, Gardner I, Golder Z, Richards FM, Kimber G, Roach A, Alderton W, Fleming A (2008) Zebrafish based assays for the assessment of cardiac, visual and gut function--potential safety screens for early drug discovery. *J Pharmacol Toxicol Methods* 58: 59-68.
45. Ton C, Lin Y, Willett C (2006) Zebrafish as a model for developmental neurotoxicity testing. *Birth Defects Res A Clin Mol Teratol* 76: 553-567.
46. McKinley ET, Baranowski TC, Blavo DO, Cato C, Doan TN, Rubinstein AL (2005) Neuroprotection of MPTP-induced toxicity in zebrafish dopaminergic neurons. *Brain Res Mol Brain Res* 141: 128-137.

47. Carvan MJ, III, Loucks E, Weber DN, Williams FE (2004) Ethanol effects on the developing zebrafish: neurobehavior and skeletal morphogenesis. *Neurotoxicol Teratol* 26: 757-768.
48. Kashyap B, Frederickson LC, Stenkamp DL (2007) Mechanisms for persistent microphthalmia following ethanol exposure during retinal neurogenesis in zebrafish embryos. *Vis Neurosci* 24: 409-421.
49. Truong L, Harper SL, Tanguay RL (2011) Evaluation of embryotoxicity using the zebrafish model. *Methods Mol Biol* 691: 271-279.
50. Peal DS, Mills RW, Lynch SN, Mosley JM, Lim E, Ellinor PT, January CT, Peterson RT, Milan DJ (2011) Novel chemical suppressors of long QT syndrome identified by an in vivo functional screen. *Circulation* 123: 23-30.
51. Methods for Measuring the Acute Toxicity of Effluents and Receiving Waters to Freshwater and Marine Organisms (2002) (EPA-821-R-02-012). Washington, DC: United States Environmental Protection Agency. 30 p.
52. Spence R, Gerlach G, Lawrence C, Smith C (2008) The behaviour and ecology of the zebrafish, *Danio rerio*. *Biol Rev Camb Philos Soc* 83: 13-34.
53. Funfak A, Brosing A, Brand M, Kohler JM (2007) Micro fluid segment technique for screening and development studies on *Danio rerio* embryos. *Lab Chip* 7: 1132-1138.
54. Shen YC, Li D, Al-Shoaibi A, Bersano-Begey T, Chen H, Ali S, Flak B, Perrin C, Winslow M, Shah H, Ramamurthy P, Schmedlen RH, Takayama S, Barald KF (2009) A student team in a University of Michigan biomedical engineering design course constructs a microfluidic bioreactor for studies of zebrafish development. *Zebrafish* 6: 201-213.
55. Braunbeck T, Boettcher M, Hollert H, Kosmehl T, Lammer E, Leist E, Rudolf M, Seitz N (2005) Towards an alternative for the acute fish LC(50) test in chemical assessment: the fish embryo toxicity test goes multi-species -- an update. *ALTEX* 22: 87-102.
56. Mizell M, Romig ES (1997) The aquatic vertebrate embryo as a sentinel for toxins: zebrafish embryo dechorionation and perivitelline space microinjection. *Int J Dev Biol* 41: 411-423.
57. Lee KJ, Nallathamby PD, Browning LM, Osgood CJ, Xu XH (2007) In vivo imaging of transport and biocompatibility of single silver nanoparticles in early development of zebrafish embryos. *ACS Nano* 1: 133-143.
58. Wang W, Liu X, Gelinas D, Ciruna B, Sun Y (2007) A fully automated robotic system for microinjection of zebrafish embryos. *PLoS ONE* 2: e862.
59. Guo S (2009) Using zebrafish to assess the impact of drugs on neural development and function. *Expert Opin Drug Discov* 4: 715-726.
60. Guo S (2004) Linking genes to brain, behavior and neurological diseases: what can we learn from zebrafish? *Genes Brain Behav* 3: 63-74.
61. Morris JA (2009) Zebrafish: a model system to examine the neurodevelopmental basis of schizophrenia. *Prog Brain Res* 179: 97-106.

62. Pogoda HM, Hammerschmidt M (2009) How to make a teleost adenohypophysis: molecular pathways of pituitary development in zebrafish. *Mol Cell Endocrinol* 312: 2-13.
63. Postlethwait JH, Woods IG, Ngo-Hazelett P, Yan YL, Kelly PD, Chu F, Huang H, Hill-Force A, Talbot WS (2000) Zebrafish comparative genomics and the origins of vertebrate chromosomes. *Genome Research* 10: 1890-1902.
64. Rodriguez F, Lopez JC, Vargas JP, Broglio C, Gomez Y, Salas C (2002) Spatial memory and hippocampal pallium through vertebrate evolution: insights from reptiles and teleost fish. *Brain Res Bull* 57: 499-503.
65. Schaaf MJ, Champagne D, van L, I, van W, Meijer AH, Meijer OC, Spaink HP, Richardson MK (2008) Discovery of a functional glucocorticoid receptor beta-isoform in zebrafish. *Endocrinology* 149: 1591-1599.
66. Sison M, Cawker J, Buske C, Gerlai R (2006) Fishing for genes influencing vertebrate behavior: zebrafish making headway. *Lab Anim (NY)* 35: 33-39.
67. Tropepe V, Sive HL (2003) Can zebrafish be used as a model to study the neurodevelopmental causes of autism? *Genes Brain Behav* 2: 268-281.
68. Veldman MB, Lin S (2008) Zebrafish as a developmental model organism for pediatric research. *Pediatr Res* 64: 470-476.
69. Steenbergen PJ, Richardson MK, Champagne DL (2010) The use of the zebrafish model in stress research. *Prog Neuropsychopharmacol Biol Psychiatry*
70. Brunelli E, Talarico E, Corapi B, Perrotta I, Tripepi S (2008) Effects of a sublethal concentration of sodium lauryl sulphate on the morphology and Na⁺/K⁺ ATPase activity in the gill of the ornate wrasse (*Thalassoma pavo*). *Ecotoxicol Environ Saf* 71: 436-445.
71. Emran F, Rihel J, Dowling JE (2008) A behavioral assay to measure responsiveness of zebrafish to changes in light intensities. *J Vis Exp*
72. Best JD, Alderton WK (2008) Zebrafish: An in vivo model for the study of neurological diseases. *Neuropsychiatr Dis Treat* 4: 567-576.
73. Kokel D, Bryan J, Laggner C, White R, Cheung CY, Mateus R, Healey D, Kim S, Werdich AA, Haggarty SJ, Macrae CA, Shoichet B, Peterson RT (2010) Rapid behavior-based identification of neuroactive small molecules in the zebrafish. *Nat Chem Biol* 6: 231-237.
74. Kokel D, Peterson RT (2008) Chemobehavioural phenomics and behaviour-based psychiatric drug discovery in the zebrafish. *Brief Funct Genomic Proteomic* 7: 483-490.
75. Drapeau P, Saint-Amant L, Buss RR, Chong M, McDearmid JR, Brustein E (2002) Development of the locomotor network in zebrafish. *Prog Neurobiol* 68: 85-111.
76. Agid Y, Buzsaki G, Diamond DM, Frackowiak R, Giedd J, Girault JA, Grace A, Lambert JJ, Manji H, Mayberg H, Popoli M, Prochiantz A, Richter-Levin G, Somogyi P, Spedding M, Svenningsson P, Weinberger D (2007) How can drug discovery for psychiatric disorders be improved? *Nat Rev Drug Discov* 6: 189-201.

77. Pariante CM (2003) Depression, stress and the adrenal axis. *J Neuroendocrinol* 15: 811-812.
78. Hasler G, Drevets WC, Manji HK, Charney DS (2004) Discovering endophenotypes for major depression. *Neuropsychopharmacology* 29: 1765-1781.
79. Holsboer F (2000) The corticosteroid receptor hypothesis of depression. *Neuropsychopharmacology* 23: 477-501.
80. Meaney MJ (2010) Epigenetics and the biological definition of gene x environment interactions. *Child Dev* 81: 41-79.
81. Heim C, Newport DJ, Mletzko T, Miller AH, Nemeroff CB (2008) The link between childhood trauma and depression: insights from HPA axis studies in humans. *Psychoneuroendocrinology* 33: 693-710.
82. Heim C, Plotsky PM, Nemeroff CB (2004) Importance of studying the contributions of early adverse experience to neurobiological findings in depression. *Neuropsychopharmacology* 29: 641-648.
83. Champagne DL, de Kloet ER, Joels M (2009) Fundamental aspects of the impact of glucocorticoids on the (immature) brain. *Semin Fetal Neonatal Med* 14: 136-142.
84. Stewart A, Wu N, Cachat J, Hart P, Gaikwad S, Wong K, Utterback E, Gilder T, Kyzar E, Newman A, Carlos D, Chang K, Hook M, Rhymes C, Caffery M, Greenberg M, Zadina J, Kalueff AV (2010) Pharmacological modulation of anxiety-like phenotypes in adult zebrafish behavioral models. *Prog Neuropsychopharmacol Biol Psychiatry*
85. Stephenson JF, Whitlock KE, Partridge JC (2011) Zebrafish preference for light or dark is dependent on ambient light levels and olfactory stimulation. *Zebrafish* 8: 17-22.
86. Maximino C, da Silva AW, Gouveia A, Jr., Herculano AM (2011) Pharmacological analysis of zebrafish (*Danio rerio*) scototaxis. *Prog Neuropsychopharmacol Biol Psychiatry* 35: 624-631.
87. Maximino C, de Brito TM, Colmanetti R, Pontes AA, de Castro HM, de Lacerda RI, Morato S, Gouveia A, Jr. (2010) Parametric analyses of anxiety in zebrafish scototaxis. *Behav Brain Res* 210: 1-7.
88. Maximino C, Marques de BT, Dias CA, Gouveia A, Jr., Morato S (2010) Scototaxis as anxiety-like behavior in fish. *Nat Protoc* 5: 209-216.
89. Lopez-Patino MA, Yu L, Cabral H, Zhdanova IV (2008) Anxiogenic effects of cocaine withdrawal in zebrafish. *Physiol Behav* 93: 160-171.
90. Levin ED, Bencan Z, Cerutti DT (2007) Anxiolytic effects of nicotine in zebrafish. *Physiol Behav* 90: 54-58.
91. Gerlai R (2010) Zebrafish antipredatory responses: a future for translational research? *Behav Brain Res* 207: 223-231.
92. Gerlai R (2010) High-throughput behavioral screens: the first step towards finding genes involved in vertebrate brain function using zebrafish. *Molecules* 15: 2609-2622.

93. Champagne DL, Hoefnagels CC, de Kloet RE, Richardson MK (2010) Translating rodent behavioral repertoire to zebrafish (*Danio rerio*): relevance for stress research. *Behav Brain Res* 214: 332-342.
94. Cachat J, Canavello P, Elegante M, Bartels B, Hart P, Bergner C, Egan R, Duncan A, Tien D, Chung A, Wong K, Goodspeed J, Tan J, Grimes C, Elkhayat S, Suci C, Rosenberg M, Chung KM, Kadri F, Roy S, Gaikwad S, Stewart A, Zapolsky I, Gilder T, Mohnot S, Beeson E, Amri H, Zukowska Z, Soignier RD, Kalueff AV (2010) Modeling withdrawal syndrome in zebrafish. *Behav Brain Res* 208: 371-376.
95. Cachat J, Stewart A, Grossman L, Gaikwad S, Kadri F, Chung KM, Wu N, Wong K, Roy S, Suci C, Goodspeed J, Elegante M, Bartels B, Elkhayat S, Tien D, Tan J, Denmark A, Gilder T, Kyzar E, Dileo J, Frank K, Chang K, Utterback E, Hart P, Kalueff AV (2010) Measuring behavioral and endocrine responses to novelty stress in adult zebrafish. *Nat Protoc* 5: 1786-1799.
96. Rihel J, Prober DA, Arvanites A, Lam K, Zimmerman S, Jang S, Haggarty SJ, Kokel D, Rubin LL, Peterson RT, Schier AF (2010) Zebrafish behavioral profiling links drugs to biological targets and rest/wake regulation. *Science* 327: 348-351.
97. Pather S, Gerlai R (2009) Shuttle box learning in zebrafish (*Danio rerio*). *Behav Brain Res* 196: 323-327.
98. Muto A, Orger MB, Wehman AM, Smear MC, Kay JN, Page-McCaw PS, Gahtan E, Xiao T, Nevin LM, Gosse NJ, Staub W, Finger-Baier K, Baier H (2005) Forward genetic analysis of visual behavior in zebrafish. *PLoS Genet* 1: e66.
99. Gutman DA, Nemeroff CB (2003) Persistent central nervous system effects of an adverse early environment: clinical and preclinical studies. *Physiol Behav* 79: 471-478.
100. Burgess HA, Granato M (2007) Modulation of locomotor activity in larval zebrafish during light adaptation. *J Exp Biol* 210: 2526-2539.
101. Berghmans S, Hunt J, Roach A, Goldsmith P (2007) Zebrafish offer the potential for a primary screen to identify a wide variety of potential anticonvulsants. *Epilepsy Res* 75: 18-28.
102. Winter MJ, Redfern WS, Hayfield AJ, Owen SF, Valentin JP, Hutchinson TH (2008) Validation of a larval zebrafish locomotor assay for assessing the seizure liability of early-stage development drugs. *J Pharmacol Toxicol Methods* 57: 176-187.
103. Richards FM, Alderton WK, Kimber GM, Liu Z, Strang I, Redfern WS, Valentin JP, Winter MJ, Hutchinson TH (2008) Validation of the use of zebrafish larvae in visual safety assessment. *J Pharmacol Toxicol Methods* 58: 50-58.
104. Sousa N, Almeida OF, Wotjak CT (2006) A hitchhiker's guide to behavioral analysis in laboratory rodents. *Genes Brain Behav* 5 Suppl 2: 5-24.
105. Bourin M, Hascoet M (2003) The mouse light/dark box test. *Eur J Pharmacol* 463: 55-65.
106. Hascoet M, Bourin M, Dhonnchadha BA (2001) The mouse light-dark paradigm: a review. *Prog Neuropsychopharmacol Biol Psychiatry* 25: 141-166.

107. Steenbergen PJ, Richardson MK, Champagne DL (2011) Patterns of avoidance behaviours in the light/dark preference test in young juvenile zebrafish: A pharmacological study. *Behav Brain Res* 222: 15-25.
108. Grossman L, Utterback E, Stewart A, Gaikwad S, Chung KM, Suci C, Wong K, Elegante M, Elkhayat S, Tan J, Gilder T, Wu N, Dileo J, Cachat J, Kalueff AV (2010) Characterization of behavioral and endocrine effects of LSD on zebrafish. *Behav Brain Res* 214: 277-284.
109. Serra EL, Medalha CC, Mattioli R (1999) Natural preference of zebrafish (*Danio rerio*) for a dark environment. *Braz J Med Biol Res* 32: 1551-1553.
110. Blaser R, Gerlai R (2006) Behavioral phenotyping in zebrafish: comparison of three behavioral quantification methods. *Behav Res Methods* 38: 456-469.
111. Prut L, Belzung C (2003) The open field as a paradigm to measure the effects of drugs on anxiety-like behaviors: a review. *Eur J Pharmacol* 463: 3-33.
112. Treit D, Fundytus M (1988) Thigmotaxis as a test for anxiolytic activity in rats. *Pharmacol Biochem Behav* 31: 959-962.
113. Sharma S, Coombs S, Patton P, Burt de PT (2009) The function of wall-following behaviors in the Mexican blind cavefish and a sighted relative, the Mexican tetra (*Astyanax*). *J Comp Physiol A Neuroethol Sens Neural Behav Physiol* 195: 225-240.
114. Simon P, Dupuis R, Costentin J (1994) Thigmotaxis as an index of anxiety in mice. Influence of dopaminergic transmissions. *Behav Brain Res* 61: 59-64.
115. Choleris E, Thomas AW, Kavaliers M, Prato FS (2001) A detailed ethological analysis of the mouse open field test: effects of diazepam, chlordiazepoxide and an extremely low frequency pulsed magnetic field. *Neurosci Biobehav Rev* 25: 235-260.
116. Champagne DL, Hoefnagels CC, de Kloet RE, Richardson MK (2010) Translating rodent behavioral repertoire to zebrafish (*Danio rerio*): Relevance for stress research. *Behav Brain Res*
117. Lopez Patino MA, Yu L, Yamamoto BK, Zhdanova IV (2008) Gender differences in zebrafish responses to cocaine withdrawal. *Physiol Behav* 95: 36-47.
118. Kallai J, Makany T, Csatho A, Karadi K, Horvath D, Kovacs-Labadi B, Jari R, Nadel L, Jacobs JW (2007) Cognitive and affective aspects of thigmotaxis strategy in humans. *Behav Neurosci* 121: 21-30.
119. Kallai J, Makany T, Karadi K, Jacobs WJ (2005) Spatial orientation strategies in Morris-type virtual water task for humans. *Behav Brain Res* 159: 187-196.
120. Henry BL, Minassian A, Young JW, Paulus MP, Geyer MA, Perry W (2010) Cross-species assessments of motor and exploratory behavior related to bipolar disorder. *Neurosci Biobehav Rev* 34: 1296-1306.
121. Wong BK, Hossain SM, Trinh E, Ottmann GA, Budaghzadeh S, Zheng QY, Simpson EM (2010) Hyperactivity, startle reactivity and cell-proliferation deficits are resistant to chronic lithium treatment in adult *Nr2e1(frc/frc)* mice. *Genes Brain Behav* 9: 681-694.

122. Kavsek M, Bornstein MH (2010) Visual habituation and dishabituation in preterm infants: a review and meta-analysis. *Res Dev Disabil* 31: 951-975.
123. Perry W, Minassian A, Paulus MP, Young JW, Kincaid MJ, Ferguson EJ, Henry BL, Zhuang X, Masten VL, Sharp RF, Geyer MA (2009) A reverse-translational study of dysfunctional exploration in psychiatric disorders: from mice to men. *Arch Gen Psychiatry* 66: 1072-1080.
124. Pugach EK, Li P, White R, Zon L (2009) Retro-orbital injection in adult zebrafish. *J Vis Exp*
125. Carvalho R, de SJ, Stockhammer OW, Savage ND, Veneman WJ, Ottenhoff TH, Dirks RP, Meijer AH, Spaink HP (2011) A high-throughput screen for tuberculosis progression. *PLoS One* 6: e16779.
126. Suster ML, Kikuta H, Urasaki A, Asakawa K, Kawakami K (2009) Transgenesis in zebrafish with the tol2 transposon system. *Methods Mol Biol* 561: 41-63.
127. Goedhart J, van WL, Hink MA, Vischer NO, Jalink K, Gadella TW, Jr. (2010) Bright cyan fluorescent protein variants identified by fluorescence lifetime screening. *Nat Methods* 7: 137-139.
128. Kremers GJ, Goedhart J, van Munster EB, Gadella TW, Jr. (2006) Cyan and yellow super fluorescent proteins with improved brightness, protein folding, and FRET Forster radius. *Biochemistry* 45: 6570-6580.
129. Shu X, Shaner NC, Yarbrough CA, Tsien RY, Remington SJ (2006) Novel chromophores and buried charges control color in mFruits. *Biochemistry* 45: 9639-9647.
130. Strack RL, Hein B, Bhattacharyya D, Hell SW, Keenan RJ, Glick BS (2009) A rapidly maturing far-red derivative of DsRed-Express2 for whole-cell labeling. *Biochemistry* 48: 8279-8281.
131. Clay H, Ramakrishnan L (2005) Multiplex fluorescent in situ hybridization in zebrafish embryos using tyramide signal amplification. *Zebrafish* 2: 105-111.
132. Welten MC, de Haan SB, van den Boogert N, Noordermeer JN, Lamers GE, Spaink HP, Meijer AH, Verbeek FJ (2006) ZebraFISH: fluorescent in situ hybridization protocol and three-dimensional imaging of gene expression patterns. *Zebrafish* 3: 465-476.
133. Brend T, Holley SA (2009) Zebrafish whole mount high-resolution double fluorescent in situ hybridization. *J Vis Exp*
134. Campos C, Kamiya M, Banala S, Johnsson K, Gonzalez-Gaitan M (2011) Labelling cell structures and tracking cell lineage in zebrafish using SNAP-tag. *Dev Dyn*
135. Spaink HP, Bagowski CP, inventors; 2009) WO/2009/056961.
136. Kaijzel EL, van der Pluijm G, Lowik CW (2007) Whole-body optical imaging in animal models to assess cancer development and progression. *Clin Cancer Res* 13: 3490-3497.
137. Schaaf MJ, Koopmans WJ, Meckel T, van NJ, Snaar-Jagalska BE, Schmidt TS, Spaink HP (2009) Single-molecule microscopy reveals membrane microdomain organization of cells in a living vertebrate. *Biophys J* 97: 1206-1214.

138. Keller PJ, Schmidt AD, Santella A, Khairy K, Bao Z, Wittbrodt J, Stelzer EH (2010) Fast, high-contrast imaging of animal development with scanned light sheet-based structured-illumination microscopy. *Nat Methods* 7: 637-642.
139. Keller PJ, Schmidt AD, Wittbrodt J, Stelzer EH (2008) Reconstruction of zebrafish early embryonic development by scanned light sheet microscopy. *Science* 322: 1065-1069.
140. Bianchini P, Diaspro A (2008) Three-dimensional (3D) backward and forward second harmonic generation (SHG) microscopy of biological tissues. *J Biophotonics* 1: 443-450.
141. Hsieh CS, Ko CY, Chen SY, Liu TM, Wu JS, Hu CH, Sun CK (2008) In vivo long-term continuous observation of gene expression in zebrafish embryo nerve systems by using harmonic generation microscopy and morphant technology. *J Biomed Opt* 13: 064041.
142. Campagnola PJ, Clark HA, Mohler WA, Lewis A, Loew LM (2001) Second-harmonic imaging microscopy of living cells. *J Biomed Opt* 6: 277-286.
143. Henriquez NV, van Overveld PG, Que I, Buijs JT, Bachelier R, Kaijzel EL, Lowik CW, Clezardin P, van der Pluijm G (2007) Advances in optical imaging and novel model systems for cancer metastasis research. *Clin Exp Metastasis* 24: 699-705.
144. Sharma R, Tsuchiya M, Tannous BA, Bartlett JD (2011) Measurement of fluoride-induced endoplasmic reticulum stress using gaussia luciferase. *Methods Enzymol* 491: 111-125.
145. Andreu N, Zelmer A, Fletcher T, Elkington PT, Ward TH, Ripoll J, Parish T, Bancroft GJ, Schaible U, Robertson BD, Wiles S (2010) Optimisation of bioluminescent reporters for use with mycobacteria. *PLoS One* 5: e10777.
146. Brannen KC, Panzica-Kelly JM, Danberry TL, Augustine-Rauch KA (2010) Development of a zebrafish embryo teratogenicity assay and quantitative prediction model. *Birth Defects Res B Dev Reprod Toxicol* 89: 66-77.
147. Arslanova D, Yang T, Xu X, Wong ST, Augelli-Szafran CE, Xia W (2010) Phenotypic analysis of images of zebrafish treated with Alzheimer's gamma-secretase inhibitors. *BMC Biotechnol* 10: 24.
148. George S, Xia T, Rallo R, Zhao Y, Ji Z, Lin S, Wang X, Zhang H, France B, Schoenfeld D, Damoiseaux R, Liu R, Lin S, Bradley KA, Cohen Y, Nel AE (2011) Use of a High-Throughput Screening Approach Coupled with In Vivo Zebrafish Embryo Screening To Develop Hazard Ranking for Engineered Nanomaterials. *ACS Nano* 5: 1805-1817.
149. Hermsen SA, van den Brandhof EJ, van der Ven LT, Piersma AH (2011) Relative embryotoxicity of two classes of chemicals in a modified zebrafish embryotoxicity test and comparison with their in vivo potencies. *Toxicol In Vitro* 25: 745-753.
150. Sawle AD, Wit E, Whale G, Cossins AR (2010) An information-rich alternative, chemicals testing strategy using a high definition toxicogenomics and zebrafish (*Danio rerio*) embryos. *Toxicol Sci* 118: 128-139.
151. Yang F, Zhang Q, Guo H, Zhang S (2010) Evaluation of cytotoxicity, genotoxicity and teratogenicity of marine sediments from Qingdao coastal areas using in vitro fish cell assay, comet assay and zebrafish embryo test. *Toxicol In Vitro* 24: 2003-2011.

152. Haffter P, Granato M, Brand M, Mullins MC, Hammerschmidt M, Kane DA, Odenthal J, van Eeden FJ, Jiang YJ, Heisenberg CP, Kelsh RN, Furutani-Seiki M, Vogelsang E, Beuchle D, Schach U, Fabian C, Nusslein-Volhard C (1996) The identification of genes with unique and essential functions in the development of the zebrafish, *Danio rerio*. *Development* 123: 1-36.
153. Mullins MC, Hammerschmidt M, Haffter P, Nusslein-Volhard C (1994) Large-scale mutagenesis in the zebrafish: in search of genes controlling development in a vertebrate. *Curr Biol* 4: 189-202.
154. Giles S, Boehm P, Brogan C, Bannigan J (2008) The effects of ethanol on CNS development in the chick embryo. *Reprod Toxicol* 25: 224-230.
155. Reimers MJ, Flockton AR, Tanguay RL (2004) Ethanol- and acetaldehyde-mediated developmental toxicity in zebrafish. *Neurotoxicol Teratol* 26: 769-781.
156. Loucks EJ, Ahlgren SC (2009) Deciphering the role of Shh signaling in axial defects produced by ethanol exposure. *Birth Defects Res A Clin Mol Teratol* 85: 556-567.
157. Carvan MJ, III, Loucks E, Weber DN, Williams FE (2004) Ethanol effects on the developing zebrafish: neurobehavior and skeletal morphogenesis. *Neurotoxicol Teratol* 26: 757-768.
158. Stromland K, Pinazo-Duran MD (2002) Ophthalmic involvement in the fetal alcohol syndrome: clinical and animal model studies. *Alcohol Alcohol* 37: 2-8.
159. Matsui JI, Egana AL, Sponholtz TR, Adolph AR, Dowling JE (2006) Effects of ethanol on photoreceptors and visual function in developing zebrafish. *Invest Ophthalmol Vis Sci* 47: 4589-4597.
160. Bilotta J, Barnett JA, Hancock L, Saszik S (2004) Ethanol exposure alters zebrafish development: a novel model of fetal alcohol syndrome. *Neurotoxicol Teratol* 26: 737-743.
161. Loucks E, Carvan MJ, III (2004) Strain-dependent effects of developmental ethanol exposure in zebrafish. *Neurotoxicol Teratol* 26: 745-755.
162. Hassel D, Scholz EP, Trano N, Friedrich O, Just S, Meder B, Weiss DL, Zitron E, Marquart S, Vogel B, Karle CA, Seemann G, Fishman MC, Katus HA, Rottbauer W (2008) Deficient zebrafish ether-a-go-go-related gene channel gating causes short-QT syndrome in zebrafish *reggae* mutants. *Circulation* 117: 866-875.
163. Mittelstadt SW, Hemenway CL, Craig MP, Hove JR (2008) Evaluation of zebrafish embryos as a model for assessing inhibition of hERG. *J Pharmacol Toxicol Methods* 57: 100-105.
164. Langheinrich U, Vacun G, Wagner T (2003) Zebrafish embryos express an orthologue of HERG and are sensitive toward a range of QT-prolonging drugs inducing severe arrhythmia. *Toxicol Appl Pharmacol* 193: 370-382.
165. Craig MP, Gilday SD, Hove JR (2006) Dose-dependent effects of chemical immobilization on the heart rate of embryonic zebrafish. *Lab Anim (NY)* 35: 41-47.
166. Forouhar AS, Hove JR, Calvert C, Flores J, Jadvar H, Gharib M (2004) Electrocardiographic characterization of embryonic zebrafish. *Conf Proc IEEE Eng Med Biol Soc* 5: 3615-3617.

167. Chi NC, Shaw RM, Jungblut B, Huisken J, Ferrer T, Arnaout R, Scott I, Beis D, Xiao T, Baier H, Jan LY, Tristani-Firouzi M, Stainier DY (2008) Genetic and physiologic dissection of the vertebrate cardiac conduction system. *PLoS Biol* 6: e109.
168. Chi NC, Bussen M, Brand-Arzamendi K, Ding C, Olgin JE, Shaw RM, Martin GR, Stainier DY (2010) Cardiac conduction is required to preserve cardiac chamber morphology. *Proc Natl Acad Sci U S A* 107: 14662-14667.
169. Berghmans S, Jette C, Langenau D, Hsu K, Stewart R, Look T, Kanki JP (2005) Making waves in cancer research: new models in the zebrafish. *Biotechniques* 39: 227-237.
170. Wattendorf DJ, Muenke M (2005) Fetal alcohol spectrum disorders. *Am Fam Physician* 72: 279-82, 285.
171. Chudley AE, Kilgour AR, Cranston M, Edwards M (2007) Challenges of diagnosis in fetal alcohol syndrome and fetal alcohol spectrum disorder in the adult. *Am J Med Genet C Semin Med Genet* 145C: 261-272.
172. Spohr HL, Willms J, Steinhausen HC (2007) Fetal alcohol spectrum disorders in young adulthood. *J Pediatr* 150: 175-9, 179.
173. Moore ES, Ward RE, Wetherill LF, Rogers JL, utti-Ramo I, Fagerlund A, Jacobson SW, Robinson LK, Hoyme HE, Mattson SN, Foroud T (2007) Unique facial features distinguish fetal alcohol syndrome patients and controls in diverse ethnic populations. *Alcohol Clin Exp Res* 31: 1707-1713.
174. Rostand A, Kaminski M, Lelong N, Dehaene P, Delestret I, Klein-Bertrand C, Querleu D, Crepin G (1990) Alcohol use in pregnancy, craniofacial features, and fetal growth. *J Epidemiol Community Health* 44: 302-306.
175. Jones KL, Smith DW (1973) Recognition of the fetal alcohol syndrome in early infancy. *Lancet* 302: 999-1001.
176. Clarren SK, Smith DW (1978) The fetal alcohol syndrome. *N Engl J Med* 298: 1063-1067.
177. Church MW, Kaltenbach JA (1997) Hearing, speech, language, and vestibular disorders in the fetal alcohol syndrome: a literature review. *Alcohol Clin Exp Res* 21: 495-512.
178. Gemma S, Vichi S, Testai E (2007) Metabolic and genetic factors contributing to alcohol induced effects and fetal alcohol syndrome. *Neurosci Biobehav Rev* 31: 221-229.
179. Bretaud S, Lee S, Guo S (2004) Sensitivity of zebrafish to environmental toxins implicated in Parkinson's disease. *Neurotoxicol Teratol* 26: 857-864.
180. Bretaud S, Allen C, Ingham PW, Bandmann O (2007) p53-dependent neuronal cell death in a DJ-1-deficient zebrafish model of Parkinson's disease. *J Neurochem* 100: 1626-1635.
181. Fleming A, Jankowski J, Goldsmith P (2010) In vivo analysis of gut function and disease changes in a zebrafish larvae model of inflammatory bowel disease: a feasibility study. *Inflamm Bowel Dis* 16: 1162-1172.

182. Liu H, Rigamonti D, Badr A, Zhang J (2011) Ccm1 regulates microvascular morphogenesis during angiogenesis. *J Vasc Res* 48: 130-140.
183. Bouvrette DJ, Sittaramane V, Heidel JR, Chandrasekhar A, Bryda EC (2010) Knockdown of bicaudal C in zebrafish (*Danio rerio*) causes cystic kidneys: a nonmammalian model of polycystic kidney disease. *Comp Med* 60: 96-106.
184. Telfer WR, Busta AS, Bonnemann CG, Feldman EL, Dowling JJ (2010) Zebrafish models of collagen VI-related myopathies. *Hum Mol Genet* 19: 2433-2444.
185. Ma AC, Fan A, Ward AC, Liongue C, Lewis RS, Cheng SH, Chan PK, Yip SF, Liang R, Leung AY (2009) A novel zebrafish jak2a(V581F) model shared features of human JAK2(V617F) polycythemia vera. *Exp Hematol* 37: 1379-1386.
186. Dutton K, Abbas L, Spencer J, Brannon C, Mowbray C, Nikaido M, Kelsh RN, Whitfield TT (2009) A zebrafish model for Waardenburg syndrome type IV reveals diverse roles for Sox10 in the otic vesicle. *Dis Model Mech* 2: 68-83.
187. Dooley KA, Fraenkel PG, Langer NB, Schmid B, Davidson AJ, Weber G, Chiang K, Foott H, Dwyer C, Wingert RA, Zhou Y, Paw BH, Zon LI (2008) montalcino, A zebrafish model for variegate porphyria. *Exp Hematol* 36: 1132-1142.
188. Haldi M, Ton C, Seng WL, McGrath P (2006) Human melanoma cells transplanted into zebrafish proliferate, migrate, produce melanin, form masses and stimulate angiogenesis in zebrafish. *Angiogenesis* 9: 139-151.
189. Kari G, Rodeck U, Dicker AP (2007) Zebrafish: an emerging model system for human disease and drug discovery. *Clin Pharmacol Ther* 82: 70-80.
190. Arenzana FJ, Carvan MJ, III, Aijon J, Sanchez-Gonzalez R, Arevalo R, Porteros A (2006) Teratogenic effects of ethanol exposure on zebrafish visual system development. *Neurotoxicol Teratol* 28: 342-348.
191. Blader P, Strahle U (1998) Ethanol impairs migration of the prechordal plate in the zebrafish embryo. *Dev Biol* 201: 185-201.
192. Meijer AH, Spaink HP (2011) Host-Pathogen Interactions Made Transparent with the Zebrafish Model. *Curr Drug Targets*
193. Ellett F, Pase L, Hayman JW, Andrianopoulos A, Lieschke GJ (2011) mpeg1 promoter transgenes direct macrophage-lineage expression in zebrafish. *Blood* 117: e49-e56.
194. Gray C, Loynes CA, Whyte MK, Crossman DC, Renshaw SA, Chico TJ (2011) Simultaneous intravital imaging of macrophage and neutrophil behaviour during inflammation using a novel transgenic zebrafish. *Thromb Haemost* 105:
195. Spaink HP, Dirks RPH inventors; (2011) High throughput method and system for in vivo screening. United States patent application WO2011/005094.
196. Teraoka H, Dong W, Hiraga T (2003) Zebrafish as a novel experimental model for developmental toxicology. *Congenit Anom (Kyoto)* 43: 123-132.

197. Labrot F, Narbonne JF, Ville P, Saint DM, Ribera D (1999) Acute toxicity, toxicokinetics, and tissue target of lead and uranium in the clam *Corbicula fluminea* and the worm *Eisenia fetida*: comparison with the fish *Brachydanio rerio*. *Arch Environ Contam Toxicol* 36: 167-178.
198. Roche H, Boge G, Peres G (1994) Acute and chronic toxicities of colchicine in *Brachydanio rerio*. *Bull Environ Contam Toxicol* 52: 69-73.
199. Zok S, Gorge G, Kalsch W, Nagel R (1991) Bioconcentration, metabolism and toxicity of substituted anilines in the zebrafish (*Brachydanio rerio*). *Sci Total Environ* 109-110: 411-421.
200. Lanzky PF, Halling-Sorensen B (1997) The toxic effect of the antibiotic metronidazole on aquatic organisms. *Chemosphere* 35: 2553-2561.
201. Kumar K, Ansari BA (1986) Malathion toxicity: effect on the liver of the fish *Brachydanio rerio* (Cyprinidae). *Ecotoxicol Environ Saf* 12: 199-205.
202. Gorge G, Nagel R (1990) Toxicity of lindane, atrazine, and deltamethrin to early life stages of zebrafish (*Brachydanio rerio*). *Ecotoxicol Environ Saf* 20: 246-255.
203. United States Environmental Protection Agency (1996) Ecological Effects Test Guidelines: OPPTS 850.1075: Fish Acute Toxicity Test, Freshwater and Marine. 1-11.
204. Peterson KJ, Lyons JB, Nowak KS, Takacs CM, Wargo MJ, McPeck MA (2004) Estimating metazoan divergence times with a molecular clock. *Proc Natl Acad Sci U S A* 101: 6536-6541.
205. McGrath P, Li CQ (2008) Zebrafish: a predictive model for assessing drug-induced toxicity. *Drug Discov Today* 13: 394-401.
206. Parng C, Seng WL, Semino C, McGrath P (2002) Zebrafish: A preclinical model for drug screening. *Assay and Drug Development Technologies* 1: 41-48.
207. Martins J, Oliva TL, Vasconcelos V (2007) Assays with *Daphnia magna* and *Danio rerio* as alert systems in aquatic toxicology. *Environ Int* 33: 414-425.
208. Halle W (2003) The Registry of Cytotoxicity: toxicity testing in cell cultures to predict acute toxicity (LD50) and to reduce testing in animals. *Altern Lab Anim* 31: 89-198.
209. Hisaoka KK (1958) The effects of 2-acetylaminofluorene on the embryonic development of the zebrafish. II. Histochemical studies. *Cancer Res* 18: 664-667.
210. Tran TC, Sneed B, Haider J, Blavo D, White A, Aiyejorun T, Baranowski TC, Rubinstein AL, Doan TN, Dingleline R, Sandberg EM (2007) Automated, quantitative screening assay for antiangiogenic compounds using transgenic zebrafish. *Cancer Res* 67: 11386-11392.
211. Canaple L, Beuf O, Armenean M, Hasserodt J, Samarut J, Janier M (2008) Fast screening of paramagnetic molecules in zebrafish embryos by MRI. *NMR Biomed* 21: 129-137.
212. George S, Xia T, Rallo R, Zhao Y, Ji Z, Lin S, Wang X, Zhang H, France B, Schoenfeld D, Damoiseaux R, Liu R, Lin S, Bradley KA, Cohen Y, Nel AE (2011) Use of a High-Throughput Screening Approach Coupled with In Vivo Zebrafish Embryo Screening To Develop Hazard Ranking for Engineered Nanomaterials. *ACS Nano*

213. Sun J, Liu J, Tu W, Xu C (2010) Separation and aquatic toxicity of enantiomers of the organophosphorus insecticide O-ethyl O-4-nitrophenyl phenylphosphonothioate (EPN). *Chemosphere* 81: 1308-1313.
214. Selderslaghs IW, Hooyberghs J, De CW, Witters HE (2010) Locomotor activity in zebrafish embryos: a new method to assess developmental neurotoxicity. *Neurotoxicol Teratol* 32: 460-471.
215. Selderslaghs IW, Van Rompay AR, De CW, Witters HE (2009) Development of a screening assay to identify teratogenic and embryotoxic chemicals using the zebrafish embryo. *Reprod Toxicol* 28: 308-320.
216. Busquet F, Nagel R, von LF, Mueller SO, Huebler N, Broschard TH (2008) Development of a new screening assay to identify proteratogenic substances using zebrafish danio rerio embryo combined with an exogenous mammalian metabolic activation system (mDarT). *Toxicol Sci* 104: 177-188.
217. Milan DJ, Peterson TA, Ruskin JN, Peterson RT, Macrae CA (2003) Drugs that induce repolarization abnormalities cause bradycardia in zebrafish. *Circulation* 107: 1355-1358.
218. Scholz EP, Niemer N, Hassel D, Zitron E, Burgers HF, Bloehs R, Seyler C, Scherer D, Thomas D, Kathofer S, Katus HA, Rottbauer WA, Karle CA (2009) Biophysical properties of zebrafish ether-a-go-go related gene potassium channels. *Biochem Biophys Res Commun* 381: 159-164.
219. Harwood HJ, Fountain D, Fountain G (1999) Economic cost of alcohol and drug abuse in the United States, 1992: a report. *Addiction* 94: 631-635.
220. Wattendorf DJ, Muenke M (2005) Fetal alcohol spectrum disorders. *Am Fam Physician* 72: 279-82, 285.
221. Rostand A, Kaminski M, Lelong N, Dehaene P, Delestret I, Klein-Bertrand C, Querleu D, Crepin G (1990) Alcohol use in pregnancy, craniofacial features, and fetal growth. *J Epidemiol Community Health* 44: 302-306.
222. Gemma S, Vichi S, Testai E (2006) Individual susceptibility and alcohol effects: biochemical and genetic aspects. *Ann Ist Super Sanita* 42: 8-16.
223. Streissguth AP, Sampson PD, Barr HM, Clarren SK, Martin DC (1986) Studying alcohol teratogenesis from the perspective of the fetal alcohol syndrome: methodological and statistical issues. *Ann N Y Acad Sci* 477: 63-86.
224. Cudd TA (2005) Animal model systems for the study of alcohol teratology. *Exp Biol Med (Maywood)* 230: 389-393.
225. Aronne MP, Evrard SG, Mirochnic S, Brusco A (2008) Prenatal ethanol exposure reduces the expression of the transcriptional factor Pax6 in the developing rat brain. *Ann N Y Acad Sci* 1139: 478-498.
226. Kaufman MH (1992) *The Atlas of Mouse Development*. London: Academic Press. 512 p.

227. Bilotta J, Saszik S, Givin CM, Hardesty HR, Sutherland SE (2002) Effects of embryonic exposure to ethanol on zebrafish visual function. *Neurotoxicol Teratol* 24: 759-766.
228. Loucks EJ, Ahlgren SC (2009) Deciphering the role of Shh signaling in axial defects produced by ethanol exposure. *Birth Defects Res A Clin Mol Teratol*
229. Carvan MJ, III, Loucks E, Weber DN, Williams FE (2004) Ethanol effects on the developing zebrafish: neurobehavior and skeletal morphogenesis. *Neurotoxicol Teratol* 26: 757-768.
230. Dlugos CA, Rabin RA (2007) Ocular deficits associated with alcohol exposure during zebrafish development. *J Comp Neurol* 502: 497-506.
231. Matsui JI, Egana AL, Sponholtz TR, Adolph AR, Dowling JE (2006) Effects of ethanol on photoreceptors and visual function in developing zebrafish. *Invest Ophthalmol Vis Sci* 47: 4589-4597.
232. Bilotta J, Barnett JA, Hancock L, Saszik S (2004) Ethanol exposure alters zebrafish development: a novel model of fetal alcohol syndrome. *Neurotoxicol Teratol* 26: 737-743.
233. Blader P, Strahle U (1998) Ethanol impairs migration of the prechordal plate in the zebrafish embryo. *Dev Biol* 201: 185-201.
234. Gerlai R, Ahmad F, Prajapati S (2008) Differences in acute alcohol-induced behavioral responses among zebrafish populations. *Alcohol Clin Exp Res* 32: 1763-1773.
235. Lockwood B, Bjerke S, Kobayashi K, Guo S (2004) Acute effects of alcohol on larval zebrafish: a genetic system for large-scale screening. *Pharmacol Biochem Behav* 77: 647-654.
236. Lele Z, Engel S, Krone PH (1997) hsp47 and hsp70 gene expression is differentially regulated in a stress- and tissue-specific manner in zebrafish embryos. *Dev Genet* 21: 123-133.
237. Li YX, Yang HT, Zdanowicz M, Sicklick JK, Qi Y, Camp TJ, Diehl AM (2007) Fetal alcohol exposure impairs Hedgehog cholesterol modification and signaling. *Laboratory investigation ; a journal of technical methods and pathology* 87: 231-240.
238. Arenzana FJ, Carvan MJ, III, Aijon J, Sanchez-Gonzalez R, Arevalo R, Porteros A (2006) Teratogenic effects of ethanol exposure on zebrafish visual system development. *Neurotoxicol Teratol* 28: 342-348.
239. Loucks EJ, Schwend T, Ahlgren SC (2007) Molecular changes associated with teratogen-induced cyclopia. *Birth Defects Res A Clin Mol Teratol* 79: 642-651.
240. Kashyap B, Frederickson LC, Stenkamp DL (2007) Mechanisms for persistent microphthalmia following ethanol exposure during retinal neurogenesis in zebrafish embryos. *Vis Neurosci* 24: 409-421.
241. Sun S, Gui Y, Wang Y, Qian L, Liu X, Jiang Q, Song H (2009) Effects of methotrexate on the developments of heart and vessel in zebrafish. *Acta Biochim Biophys Sin (Shanghai)* 41: 86-96.
242. Sun SN, Gui YH, Wang YX, Qian LX, Jiang Q, Liu D, Song HY (2007) Effect of dihydrofolate reductase gene knock-down on the expression of heart and neural crest derivatives

expressed transcript 2 in zebrafish cardiac development. *Chin Med J (Engl)* 120: 1166-1171.

243. Fan CY, Cowden J, Simmons SO, Padilla S, Ramabhadran R (2009) Gene expression changes in developing zebrafish as potential markers for rapid developmental neurotoxicity screening. *Neurotoxicol Teratol*
244. Thisse C, Thisse B (2008) High-resolution in situ hybridization to whole-mount zebrafish embryos. *Nat Protoc* 3: 59-69.
245. Brand M, Heisenberg CP, Jiang YJ, Beuchle D, Lun K, Furutani-Seiki M, Granato M, Haffter P, Hammerschmidt M, Kane DA, Kelsh RN, Mullins MC, Odenthal J, van Eeden FJ, Nusslein-Volhard C (1996) Mutations in zebrafish genes affecting the formation of the boundary between midbrain and hindbrain. *Development* 123: 179-190.
246. Sulik KK (1984) Critical periods for alcohol teratogenesis in mice, with special reference to the gastrulation stage of embryogenesis. *Ciba Found Symp* 105: 124-141.
247. Maier SE, Chen WJ, West JR (1996) Prenatal binge-like alcohol exposure alters neurochemical profiles in fetal rat brain. *Pharmacol Biochem Behav* 55: 521-529.
248. Maier SE, West JR (2001) Drinking patterns and alcohol-related birth defects. *Alcohol Res Health* 25: 168-174.
249. Nayak RB, Murthy P (2008) Fetal alcohol spectrum disorder. *Indian Pediatr* 45: 977-983.
250. Reimers MJ, Hahn ME, Tanguay RL (2004) Two zebrafish alcohol dehydrogenases share common ancestry with mammalian class I, II, IV, and V alcohol dehydrogenase genes but have distinct functional characteristics. *J Biol Chem* 279: 38303-38312.
251. Haycock PC (2009) Fetal alcohol spectrum disorders: the epigenetic perspective. *Biol Reprod* 81: 607-617.
252. Ang HL, Deltour L, Hayamizu TF, Zgombic-Knight M, Duester G (1996) Retinoic acid synthesis in mouse embryos during gastrulation and craniofacial development linked to class IV alcohol dehydrogenase gene expression. *J Biol Chem* 271: 9526-9534.
253. Peng J, Wagle M, Mueller T, Mathur P, Lockwood BL, Bretaud S, Guo S (2009) Ethanol-modulated camouflage response screen in zebrafish uncovers a novel role for cAMP and extracellular signal-regulated kinase signaling in behavioral sensitivity to ethanol. *J Neurosci* 29: 8408-8418.
254. Fujii R (2000) The regulation of motile activity in fish chromatophores. *Pigment Cell Res* 13: 300-319.
255. Høglund E, Balm PH, Winberg S (2000) Skin darkening, a potential social signal in subordinate arctic charr (*Salvelinus alpinus*): the regulatory role of brain monoamines and pro-opiomelanocortin-derived peptides. *J Exp Biol* 203: 1711-1721.
256. Ahlgren SC, Thakur V, Bronner-Fraser M (2002) Sonic hedgehog rescues cranial neural crest from cell death induced by ethanol exposure. *Proc Natl Acad Sci U S A* 99: 10476-10481.

257. Birkholz DA, Killian EC, George KM, Artinger KB (2009) Prdm1a is necessary for posterior pharyngeal arch development in zebrafish. *Dev Dyn* 238: 2575-2587.
258. Drerup CM, Wiora HM, Topczewski J, Morris JA (2009) Disc1 regulates foxd3 and sox10 expression, affecting neural crest migration and differentiation. *Development* 136: 2623-2632.
259. Sperber SM, Saxena V, Hatch G, Ekker M (2008) Zebrafish dlx2a contributes to hindbrain neural crest survival, is necessary for differentiation of sensory ganglia and functions with dlx1a in maturation of the arch cartilage elements. *Dev Biol* 314: 59-70.
260. Miller CT, Yelon D, Stainier DY, Kimmel CB (2003) Two endothelin 1 effectors, hand2 and bapx1, pattern ventral pharyngeal cartilage and the jaw joint. *Development* 130: 1353-1365.
261. Chen YH, Lin YT, Lee GH (2009) Novel and unexpected functions of zebrafish CCAAT box binding transcription factor (NF-Y) B subunit during cartilages development. *Bone* 44: 777-784.
262. Ekker M, Akimenko MA, Allende ML, Smith R, Drouin G, Langille RM, Weinberg ES, Westerfield M (1997) Relationships among msx gene structure and function in zebrafish and other vertebrates. *Mol Biol Evol* 14: 1008-1022.
263. Akimenko MA, Ekker M, Wegner J, Lin W, Westerfield M (1994) Combinatorial expression of three zebrafish genes related to distal-less: part of a homeobox gene code for the head. *J Neurosci* 14: 3475-3486.
264. Thomas BL, Tucker AS, Qui M, Ferguson CA, Hardcastle Z, Rubenstein JL, Sharpe PT (1997) Role of Dlx-1 and Dlx-2 genes in patterning of the murine dentition. *Development* 124: 4811-4818.
265. Thomas T, Kurihara H, Yamagishi H, Kurihara Y, Yazaki Y, Olson EN, Srivastava D (1998) A signaling cascade involving endothelin-1, dHAND and msx1 regulates development of neural-crest-derived branchial arch mesenchyme. *Development* 125: 3005-3014.
266. Satokata I, Maas R (1994) Msx1 deficient mice exhibit cleft palate and abnormalities of craniofacial and tooth development. *Nat Genet* 6: 348-356.
267. Eberhart JK, Swartz ME, Crump JG, Kimmel CB (2006) Early Hedgehog signaling from neural to oral epithelium organizes anterior craniofacial development. *Development* 133: 1069-1077.
268. Jeong J, Mao J, Tenzen T, Kottmann AH, McMahon AP (2004) Hedgehog signaling in the neural crest cells regulates the patterning and growth of facial primordia. *Genes Dev* 18: 937-951.
269. Wentzel P, Eriksson UJ (2009) Altered gene expression in neural crest cells exposed to ethanol in vitro. *Brain Res*
270. Kily LJ, Cowe YC, Hussain O, Patel S, McElwaine S, Cotter FE, Brennan CH (2008) Gene expression changes in a zebrafish model of drug dependency suggest conservation of neuro-adaptation pathways. *J Exp Biol* 211: 1623-1634.

271. Calloni GW, Glavieux-Pardanaud C, Le Douarin NM, Dupin E (2007) Sonic Hedgehog promotes the development of multipotent neural crest progenitors endowed with both mesenchymal and neural potentials. *Proc Natl Acad Sci U S A* 104: 19879-19884.
272. Waldo K, Miyagawa-Tomita S, Kumiski D, Kirby ML (1998) Cardiac neural crest cells provide new insight into septation of the cardiac outflow tract: aortic sac to ventricular septal closure. *Dev Biol* 196: 129-144.
273. Le Douarin NM, Brito JM, Creuzet S (2007) Role of the neural crest in face and brain development. *Brain Res Rev* 55: 237-247.
274. Sulik KK, Johnston MC, Daft PA, Russell WE, Dehart DB (1986) Fetal alcohol syndrome and DiGeorge anomaly: critical ethanol exposure periods for craniofacial malformations as illustrated in an animal model. *Am J Med Genet Suppl* 2: 97-112.
275. Sulik KK, Johnston MC, Webb MA (1981) Fetal alcohol syndrome: embryogenesis in a mouse model. *Science* 214: 936-938.
276. Chen SY, Periasamy A, Yang B, Herman B, Jacobson K, Sulik KK (2000) Differential sensitivity of mouse neural crest cells to ethanol-induced toxicity. *Alcohol* 20: 75-81.
277. Hall C, Flores MV, Murison G, Crosier K, Crosier P (2006) An essential role for zebrafish *Fgfr1* during gill cartilage development. *Mech Dev* 123: 925-940.
278. Blentic A, Tandon P, Payton S, Walshe J, Carney T, Kelsh RN, Mason I, Graham A (2008) The emergence of ectomesenchyme. *Dev Dyn* 237: 592-601.
279. Hong SK, Tsang M, Dawid IB (2008) The *mych* gene is required for neural crest survival during zebrafish development. *PLoS ONE* 3: e2029.
280. Yeo GH, Cheah FS, Jabs EW, Chong SS (2007) Zebrafish *twist1* is expressed in craniofacial, vertebral, and renal precursors. *Dev Genes Evol* 217: 783-789.
281. Gautier P, Naranjo-Golborne C, Taylor MS, Jackson IJ, Smyth I (2008) Expression of the *fras1/frem* gene family during zebrafish development and fin morphogenesis. *Dev Dyn* 237: 3295-3304.
282. Knight RD, Schilling TF (2006) Cranial neural crest and development of the head skeleton. *Adv Exp Med Biol* 589: 120-133.
283. Renvoize C, Biola A, Pallardy M, Breard J (1998) Apoptosis: identification of dying cells. *Cell Biol Toxicol* 14: 111-120.
284. Cartwright MM, Smith SM (1995) Increased cell death and reduced neural crest cell numbers in ethanol-exposed embryos: partial basis for the fetal alcohol syndrome phenotype. *Alcohol Clin Exp Res* 19: 378-386.
285. Cartwright MM, Smith SM (1995) Stage-dependent effects of ethanol on cranial neural crest cell development: partial basis for the phenotypic variations observed in fetal alcohol syndrome. *Alcohol Clin Exp Res* 19: 1454-1462.

286. Dunty WC, Jr., Chen SY, Zucker RM, Dehart DB, Sulik KK (2001) Selective vulnerability of embryonic cell populations to ethanol-induced apoptosis: implications for alcohol-related birth defects and neurodevelopmental disorder. *Alcohol Clin Exp Res* 25: 1523-1535.
287. Kotch LE, Sulik KK (1992) Experimental fetal alcohol syndrome: proposed pathogenic basis for a variety of associated facial and brain anomalies. *Am J Med Genet* 44: 168-176.
288. Giles S, Boehm P, Brogan C, Bannigan J (2008) The effects of ethanol on CNS development in the chick embryo. *Reprod Toxicol* 25: 224-230.
289. Waldo K, Miyagawa-Tomita S, Kumiski D, Kirby ML (1998) Cardiac neural crest cells provide new insight into septation of the cardiac outflow tract: aortic sac to ventricular septal closure. *Dev Biol* 196: 129-144.
290. Le Douarin NM, Brito JM, Creuzet S (2007) Role of the neural crest in face and brain development. *Brain Res Rev* 55: 237-247.
291. Sulik KK, Johnston MC, Daft PA, Russell WE, Dehart DB (1986) Fetal alcohol syndrome and DiGeorge anomaly: critical ethanol exposure periods for craniofacial malformations as illustrated in an animal model. *Am J Med Genet Suppl* 2: 97-112.
292. Sulik KK, Johnston MC, Webb MA (1981) Fetal alcohol syndrome: embryogenesis in a mouse model. *Science* 214: 936-938.
293. Chen SY, Periasamy A, Yang B, Herman B, Jacobson K, Sulik KK (2000) Differential sensitivity of mouse neural crest cells to ethanol-induced toxicity. *Alcohol* 20: 75-81.
294. Hall C, Flores MV, Murison G, Crosier K, Crosier P (2006) An essential role for zebrafish *Fgfr1* during gill cartilage development. *Mech Dev* 123: 925-940.
295. Akimenko MA, Ekker M, Wegner J, Lin W, Westerfield M (1994) Combinatorial expression of three zebrafish genes related to *distal-less*: part of a homeobox gene code for the head. *J Neurosci* 14: 3475-3486.
296. Blentic A, Tandon P, Payton S, Walshe J, Carney T, Kelsh RN, Mason I, Graham A (2008) The emergence of ectomesenchyme. *Dev Dyn* 237: 592-601.
297. Hong SK, Tsang M, Dawid IB (2008) The *mych* gene is required for neural crest survival during zebrafish development. *PLoS ONE* 3: e2029.
298. Yeo GH, Cheah FS, Jabs EW, Chong SS (2007) Zebrafish *twist1* is expressed in craniofacial, vertebral, and renal precursors. *Dev Genes Evol* 217: 783-789.
299. Gautier P, Naranjo-Golborne C, Taylor MS, Jackson IJ, Smyth I (2008) Expression of the *fras1/frem* gene family during zebrafish development and fin morphogenesis. *Dev Dyn* 237: 3295-3304.
300. Knight RD, Schilling TF (2006) Cranial neural crest and development of the head skeleton. *Adv Exp Med Biol* 589: 120-133.

301. Birkholz DA, Olesnicky Killian EC, George KM, Artinger KB (2009) Prdm1a is necessary for posterior pharyngeal arch development in zebrafish. *Dev Dyn* 238: 2575-2587.
302. Drerup CM, Wiora HM, Topczewski J, Morris JA (2009) Disc1 regulates foxd3 and sox10 expression, affecting neural crest migration and differentiation. *Development* 136: 2623-2632.
303. Sulik KK, Cook CS, Webster WS (1988) Teratogens and craniofacial malformations: relationships to cell death. *Development* 103 Suppl: 213-231.
304. Cartwright MM, Smith SM (1995) Increased cell death and reduced neural crest cell numbers in ethanol-exposed embryos: partial basis for the fetal alcohol syndrome phenotype. *Alcohol Clin Exp Res* 19: 378-386.
305. Rovasio RA, Battiato NL (2002) Ethanol induces morphological and dynamic changes on in vivo and in vitro neural crest cells. *Alcohol Clin Exp Res* 26: 1286-1298.
306. Barnes DM (1986) Tight money squeezes out animal models. *Science* 232: 309-311.
307. Verkman AS (2004) Drug discovery in academia. *Am J Physiol Cell Physiol* 286: C465-C474.
308. Dove A (1999) Drug screening--beyond the bottleneck. *Nat Biotechnol* 17: 859-863.
309. Pardo-Martin C, Chang TY, Koo BK, Gilleland CL, Wasserman SC, Yanik MF (2010) High-throughput in vivo vertebrate screening. *Nat Methods* 7: 634-636.
310. Melin J, Lee A, Foygel K, Leong DE, Quake SR, Yao MW (2009) In vitro embryo culture in defined, sub-microliter volumes. *Dev Dyn* 238: 950-955.
311. Rohde CB, Zeng F, Gonzalez-Rubio R, Angel M, Yanik MF (2007) Microfluidic system for on-chip high-throughput whole-animal sorting and screening at subcellular resolution. *Proc Natl Acad Sci U S A* 104: 13891-13895.
312. Wereley ST, Meinhart CD (2010) Recent advances in micro-particle image velocimetry. *Annu Rev Fluid Mech* 42: 557-576.
313. Poelma C, Van der Heiden K, Hierck BP, Poelmann RE, Westerweel J (2010) Measurements of the wall shear stress distribution in the outflow tract of an embryonic chicken heart. *J R Soc Interface* 7: 91-103.
314. Fraysse B, Mons R, Garric J (2006) Development of a zebrafish 4-day embryo-larval bioassay to assess toxicity of chemicals. *Ecotoxicol Environ Saf* 63: 253-267.
315. Hoglund E, Balm PH, Winberg S (2000) Skin darkening, a potential social signal in subordinate arctic charr (*Salvelinus alpinus*): the regulatory role of brain monoamines and pro-opiomelanocortin-derived peptides. *J Exp Biol* 203: 1711-1721.
316. Peng J, Wagle M, Mueller T, Mathur P, Lockwood BL, Bretaud S, Guo S (2009) Ethanol-modulated camouflage response screen in zebrafish uncovers a novel role for cAMP and extracellular signal-regulated kinase signaling in behavioral sensitivity to ethanol. *J Neurosci* 29: 8408-8418.

317. Tanguay RL, Reimers MJ (2008) Analysis of ethanol developmental toxicity in zebrafish. *Methods Mol Biol* 447: 63-74.
318. Reimers MJ, Flockton AR, Tanguay RL (2004) Ethanol- and acetaldehyde-mediated developmental toxicity in zebrafish. *Neurotoxicol Teratol* 26: 769-781.
319. Hallare A, Nagel K, Kohler HR, Triebkorn R (2006) Comparative embryotoxicity and proteotoxicity of three carrier solvents to zebrafish (*Danio rerio*) embryos. *Ecotoxicol Environ Saf* 63: 378-388.
320. Stachowiak JC, Shugard EE, Mosier BP, Renzi RF, Caton PF, Ferko SM, Van de Vreugde JL, Yee DD, Haroldsen BL, VanderNoot VA (2007) Autonomous microfluidic sample preparation system for protein profile-based detection of aerosolized bacterial cells and spores. *Anal Chem* 79: 5763-5770.
321. Lawson ND, Weinstein BM (2002) In vivo imaging of embryonic vascular development using transgenic zebrafish. *Dev Biol* 248: 307-318.
322. Voelker D, Vess C, Tillmann M, Nagel R, Otto GW, Geisler R, Schirmer K, Scholz S (2007) Differential gene expression as a toxicant-sensitive endpoint in zebrafish embryos and larvae. *Aquat Toxicol* 81: 355-364.
323. Lammer E, Carr GJ, Wendler K, Rawlings JM, Belanger SE, Braunbeck T (2009) Is the fish embryo toxicity test (FET) with the zebrafish (*Danio rerio*) a potential alternative for the fish acute toxicity test? *Comp Biochem Physiol C Toxicol Pharmacol* 149: 196-209.
324. Hill AJ, Teraoka H, Heideman W, Peterson RE (2005) Zebrafish as a model vertebrate for investigating chemical toxicity. *Toxicol Sci* 86: 6-19.
325. Truong L, Harper SL, Tanguay RL (2011) Evaluation of embryotoxicity using the zebrafish model. *Methods Mol Biol* 691: 271-279.
326. Bai W, Tian W, Zhang Z, He X, Ma Y, Liu N, Chai Z (2010) Effects of copper nanoparticles on the development of zebrafish embryos. *J Nanosci Nanotechnol* 10: 8670-8676.
327. Hu N, Yost HJ, Clark EB (2001) Cardiac morphology and blood pressure in the adult zebrafish. *Anat Rec* 264: 1-12.
328. Mizell M, Romig ES (1997) The aquatic vertebrate embryo as a sentinel for toxins: zebrafish embryo dechoriation and perivitelline space microinjection. *Int J Dev Biol* 41: 411-423.
329. Henn K, Braunbeck T (2011) Dechoriation as a tool to improve the fish embryo toxicity test (FET) with the zebrafish (*Danio rerio*). *Comp Biochem Physiol C Toxicol Pharmacol* 153: 91-98.
330. Braunbeck T, Boettcher M, Hollert H, Kosmehl T, Lammer E, Leist E, Rudolf M, Seitz N (2005) Towards an alternative for the acute fish LC(50) test in chemical assessment: the fish embryo toxicity test goes multi-species -- an update. *ALTEX* 22: 87-102.
331. McKim JM, Eaton JG, Holcombe GW (1978) Metal toxicity to embryos and larvae of eight species of freshwater fish-II: copper. *Bull Environ Contam Toxicol* 19: 608-616.

332. Shazili NA, Pascoe D (1986) Variable sensitivity of rainbow trout (*Salmo gairdneri*) eggs and alevins to heavy metals. *Bull Environ Contam Toxicol* 36: 468-474.
333. Barbara C. Scudder JLCaHVL (1988) Effects of copper on development of the fathead minnow, *Pimephales promelas* Rafinesque. *Aquatic Toxicology* 12: 107-124.
334. Eyckmans M, Tudorache C, Darras VM, Blust R, De BG (2010) Hormonal and ion regulatory response in three freshwater fish species following waterborne copper exposure. *Comp Biochem Physiol C Toxicol Pharmacol* 152: 270-278.
335. Rogers JT, Richards JG, Wood CM (2003) Ionoregulatory disruption as the acute toxic mechanism for lead in the rainbow trout (*Oncorhynchus mykiss*). *Aquat Toxicol* 64: 215-234.
336. Craven R (2011) The risky business of drug development in neurology. *Lancet Neurol* 10: 116-117.
337. Parng C, Seng WL, Semino C, McGrath P (2002) Zebrafish: a preclinical model for drug screening. *Assay Drug Dev Technol* 1: 41-48.
338. Selderslaghs IW, Blust R, Witters HE (2011) Feasibility study of the zebrafish assay as an alternative method to screen for developmental toxicity and embryotoxicity using a training set of 27 compounds. *Reprod Toxicol*
339. Ali S, Champagne DL, Spaink HP, Richardson MK (2011) Zebrafish embryos and larvae: A new generation of disease models and drug screens. *Birth Defects Res C Embryo Today* 93: 115-133.
340. Sylvain NJ, Brewster DL, Ali DW (2010) Zebrafish embryos exposed to alcohol undergo abnormal development of motor neurons and muscle fibers. *Neurotoxicol Teratol* 32: 472-480.
341. Scholz S, Fischer S, Gundel U, Kuster E, Luckenbach T, Voelker D (2008) The zebrafish embryo model in environmental risk assessment--applications beyond acute toxicity testing. *Environ Sci Pollut Res Int* 15: 394-404.
342. Champagne DL, Hoefnagels CC, de Kloet RE, Richardson MK (2010) Translating rodent behavioral repertoire to zebrafish (*Danio rerio*): relevance for stress research. *Behav Brain Res* 214: 332-342.
343. Rihel J, Prober DA, Arvanites A, Lam K, Zimmerman S, Jang S, Haggarty SJ, Kokel D, Rubin LL, Peterson RT, Schier AF (2010) Zebrafish behavioral profiling links drugs to biological targets and rest/wake regulation. *Science* 327: 348-351.
344. Burne T, Scott E, van SB, Hilliard M, Reinhard J, Claudianos C, Eyles D, McGrath J (2011) Big ideas for small brains: what can psychiatry learn from worms, flies, bees and fish? *Mol Psychiatry* 16: 7-16.
345. Guo S (2004) Linking genes to brain, behavior and neurological diseases: what can we learn from zebrafish? *Genes Brain Behav* 3: 63-74.
346. Lieschke GJ, Currie PD (2007) Animal models of human disease: zebrafish swim into view. *Nat Rev Genet* 8: 353-367.

347. Postlethwait JH, Woods IG, Ngo-Hazelett P, Yan YL, Kelly PD, Chu F, Huang H, Hill-Force A, Talbot WS (2000) Zebrafish comparative genomics and the origins of vertebrate chromosomes. *Genome Res* 10: 1890-1902.
348. Tropepe V, Sive HL (2003) Can zebrafish be used as a model to study the neurodevelopmental causes of autism? *Genes Brain Behav* 2: 268-281.
349. Veldman MB, Lin S (2008) Zebrafish as a developmental model organism for pediatric research. *Pediatr Res* 64: 470-476.
350. Brustein E, Saint-Amant L, Buss RR, Chong M, McDearmid JR, Drapeau P (2003) Steps during the development of the zebrafish locomotor network. *J Physiol Paris* 97: 77-86.
351. Drapeau P, Saint-Amant L, Buss RR, Chong M, McDearmid JR, Brustein E (2002) Development of the locomotor network in zebrafish. *Prog Neurobiol* 68: 85-111.
352. McLean DL, Fetcho JR (2004) Ontogeny and innervation patterns of dopaminergic, noradrenergic, and serotonergic neurons in larval zebrafish. *J Comp Neurol* 480: 38-56.
353. Wullimann MF, Mueller T (2004) Teleostean and mammalian forebrains contrasted: Evidence from genes to behavior. *J Comp Neurol* 475: 143-162.
354. Panula P, Chen YC, Priyadarshini M, Kudo H, Semenova S, Sundvik M, Sallinen V (2010) The comparative neuroanatomy and neurochemistry of zebrafish CNS systems of relevance to human neuropsychiatric diseases. *Neurobiol Dis* 40: 46-57.
355. Kaslin J, Panula P (2001) Comparative anatomy of the histaminergic and other aminergic systems in zebrafish (*Danio rerio*). *J Comp Neurol* 440: 342-377.
356. Parker B, Connaughton VP (2007) Effects of nicotine on growth and development in larval zebrafish. *Zebrafish* 4: 59-68.
357. Rink E, Wullimann MF (2001) The teleostean (zebrafish) dopaminergic system ascending to the subpallium (striatum) is located in the basal diencephalon (posterior tuberculum). *Brain Res* 889: 316-330.
358. Agetsuma M, Aizawa H, Aoki T, Nakayama R, Takahoko M, Goto M, Sassa T, Amo R, Shiraki T, Kawakami K, Hosoya T, Higashijima S, Okamoto H (2010) The habenula is crucial for experience-dependent modification of fear responses in zebrafish. *Nat Neurosci* 13: 1354-1356.
359. The Merck index (2006): An encyclopedia of chemicals, drugs, and biologicals. 14th ed.: pp1-1156.
360. Sansone F, Rossi A, Del GP, De SF, Aquino RP, Lauro MR (2009) Hesperidin gastroresistant microparticles by spray-drying: preparation, characterization, and dissolution profiles. *AAPS PharmSciTech* 10: 391-401.
361. Kometani T, Nishimura T, Nakae T, Takii H, Okada S (1996) Synthesis of neohesperidin glycosides and naringin glycosides by cyclodextrin glucanotransferase from an alkalophilic *Bacillus* species. *Biosci Biotechnol Biochem* 60: 645-649.

362. Emran F, Rihel J, Dowling JE (2008) A behavioral assay to measure responsiveness of zebrafish to changes in light intensities. *J Vis Exp*
363. Sipos ML, Burchnell V, Galbicka G (1999) Dose-response curves and time-course effects of selected anticholinergics on locomotor activity in rats. *Psychopharmacology (Berl)* 147: 250-256.
364. Friese J, Gleitz J, Gutser UT, Heubach JF, Matthiesen T, Wilffert B, Selve N (1997) Aconitum sp. alkaloids: the modulation of voltage-dependent Na⁺ channels, toxicity and antinociceptive properties. *Eur J Pharmacol* 337: 165-174.
365. Kulkarni SK, Dhir A (2008) On the mechanism of antidepressant-like action of berberine chloride. *Eur J Pharmacol* 589: 163-172.
366. Kulkarni SK, Dhir A (2007) Possible involvement of L-arginine-nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) signaling pathway in the antidepressant activity of berberine chloride. *Eur J Pharmacol* 569: 77-83.
367. Won M, Minabe Y, Tani K, Suzuki K, Kawai M, Sekine Y, Ashby CR, Jr., Takei N, Mori N (2003) The effects of dentate granule cell destruction on behavioral activity and Fos protein expression induced by systemic MDMA in rats. *Neurosci Res* 46: 153-160.
368. Tandon P, McLamb RL, Novicki D, Shuey DL, Tilson HA (1988) Fetal hippocampal cell suspensions ameliorate behavioral effects of intradentate colchicine in the rat. *Brain Res* 473: 241-248.
369. Arihan O, Boz M, Iskit AB, Ilhan M (2009) Antinociceptive activity of coniine in mice. *J Ethnopharmacol* 125: 274-278.
370. Harrod SB, Van Horn ML (2009) Sex differences in tolerance to the locomotor depressant effects of lobeline in periadolescent rats. *Pharmacol Biochem Behav* 94: 296-304.
371. Airavaara M, Tuomainen H, Piepponen TP, Saarma M, Ahtee L (2007) Effects of repeated morphine on locomotion, place preference and dopamine in heterozygous glial cell line-derived neurotrophic factor knockout mice. *Genes Brain Behav* 6: 287-298.
372. Macphail RC, Farmer JD, Jarema KA (2007) Effects of acute and weekly episodic exposures to anatoxin-a on the motor activity of rats: comparison with nicotine. *Toxicology* 234: 83-89.
373. Nassiri-Asl M, Zamansoltani F, Torabinejad B (2009) Antiepileptic effects of quinine in the pentylenetetrazole model of seizure. *Seizure* 18: 129-132.
374. Himmel HM (2008) Safety pharmacology assessment of central nervous system function in juvenile and adult rats: effects of pharmacological reference compounds. *J Pharmacol Toxicol Methods* 58: 129-146.
375. Bruno KJ, Hess EJ (2006) The alpha(2C)-adrenergic receptor mediates hyperactivity of coloboma mice, a model of attention deficit hyperactivity disorder. *Neurobiol Dis* 23: 679-688.
376. Yan JJ, Kim DH, Moon YS, Jung JS, Ahn EM, Baek NI, Song DK (2004) Protection against beta-amyloid peptide-induced memory impairment with long-term administration of extract

of *Angelica gigas* or decursinol in mice. *Prog Neuropsychopharmacol Biol Psychiatry* 28: 25-30.

377. Ainsah O, Nabishah BM, Osman CB, Khalid BA (1999) Effects of naloxone, glycyrrhizic acid, dexamethasone and deoxycorticosterone in repetitive stress. *Clin Exp Pharmacol Physiol* 26: 433-437.
378. Ainsah O, Nabishah BM, Osman CB, Khalid BA (1999) Short- and long-term effects of glycyrrhizic acid in repetitive stress. *Clin Exp Pharmacol Physiol* 26: 444-448.
379. Loscalzo LM, Wasowski C, Paladini AC, Marder M (2008) Opioid receptors are involved in the sedative and antinociceptive effects of hesperidin as well as in its potentiation with benzodiazepines. *Eur J Pharmacol* 580: 306-313.
380. Fernandez SP, Wasowski C, Loscalzo LM, Granger RE, Johnston GA, Paladini AC, Marder M (2006) Central nervous system depressant action of flavonoid glycosides. *Eur J Pharmacol* 539: 168-176.
381. Doggett NS, Spencer PS (1971) Pharmacological properties of centrally administered ouabain and their modification by other drugs. *Br J Pharmacol* 42: 242-253.
382. Lukawski K, Nieradko B, Sieklucka-Dziuba M (2005) Effects of cadmium on memory processes in mice exposed to transient cerebral oligemia. *Neurotoxicol Teratol* 27: 575-584.
383. Correa M, Sanchis-Segura C, Aragon CM (2001) Brain catalase activity is highly correlated with ethanol-induced locomotor activity in mice. *Physiol Behav* 73: 641-647.
384. Correa M, Miquel M, Aragon CM (2000) Lead acetate potentiates brain catalase activity and enhances ethanol-induced locomotion in mice. *Pharmacol Biochem Behav* 66: 137-142.
385. Tomasiewicz HC, Mague SD, Cohen BM, Carlezon WA, Jr. (2006) Behavioral effects of short-term administration of lithium and valproic acid in rats. *Brain Res* 1093: 83-94.
386. Waller MB, Murphy JM, McBride WJ, Lumeng L, Li TK (1986) Effect of low dose ethanol on spontaneous motor activity in alcohol-preferring and -nonpreferring lines of rats. *Pharmacol Biochem Behav* 24: 617-623.
387. Castro CA, Hogan JB, Benson KA, Shehata CW, Landauer MR (1995) Behavioral effects of vehicles: DMSO, ethanol, Tween-20, Tween-80, and emulphor-620. *Pharmacol Biochem Behav* 50: 521-526.
388. Preache MM, Gibson JE (1976) Effects of cyclophosphamide treatment of newborn mice on the development of swimming and reflex behavior and on adult behavioral performance. *Dev Psychobiol* 9: 555-567.
389. Millecamps M, Etienne M, Jourdan D, Eschaliere A, Ardid D (2004) Decrease in non-selective, non-sustained attention induced by a chronic visceral inflammatory state as a new pain evaluation in rats. *Pain* 109: 214-224.
390. Boyd EM, Hottenroth SM (1968) The toxicity of phenacetin at the range of the oral LD50(100 days) in albino rats. *Toxicol Appl Pharmacol* 12: 80-93.

391. Mihara T, Iwashita A, Matsuoka N (2008) A novel adenosine A(1) and A(2A) receptor antagonist ASP5854 ameliorates motor impairment in MPTP-treated marmosets: comparison with existing anti-Parkinson's disease drugs. *Behav Brain Res* 194: 152-161.
392. Bisong SA, Brown R, Osim EE (2010) Comparative effects of Rauwolfia vomitoria and chlorpromazine on locomotor behaviour and anxiety in mice. *J Ethnopharmacol* 132: 334-339.
393. Shekhar A, DiMicco JA (1987) Defense reaction elicited by injection of GABA antagonists and synthesis inhibitors into the posterior hypothalamus in rats. *Neuropharmacology* 26: 407-417.
394. Fredriksson A, Palomo T, Archer T (2000) Effects of MAO inhibitors upon MPTP mice chronically treated with suprathreshold doses of L-dopa. *Behav Pharmacol* 11: 571-581.
395. Balino P, Pastor R, Aragon CM (2010) Participation of L-type calcium channels in ethanol-induced behavioral stimulation and motor incoordination: effects of diltiazem and verapamil. *Behav Brain Res* 209: 196-204.
396. Sanchis-Segura C, Miquel M, Correa M, Aragon CM (1999) The catalase inhibitor sodium azide reduces ethanol-induced locomotor activity. *Alcohol* 19: 37-42.
397. Lalonde R, Joyal CC, Beaudin S (1997) Effects of sodium azide on motor activity, motor coordination, and learning. *Pharmacol Biochem Behav* 56: 67-71.
398. Malek FA, Moritz KU, Fanghanel J (2004) Effects of a single inhalative exposure to formaldehyde on the open field behavior of mice. *Int J Hyg Environ Health* 207: 151-158.
399. Malek FA, Moritz KU, Fanghanel J (2003) Formaldehyde inhalation & open field behaviour in rats. *Indian J Med Res* 118: 90-96.
400. Buckley JP, Solaro RJ, Barry H, III (1969) Effects of phenformin HC1 on rats subjected to simulated high altitude. *J Pharm Sci* 58: 348-351.
401. Dhir A, Kulkarni SK (2007) Involvement of dopamine (DA)/serotonin (5-HT)/sigma (sigma) receptor modulation in mediating the antidepressant action of ropinirole hydrochloride, a D2/D3 dopamine receptor agonist. *Brain Res Bull* 74: 58-65.
402. Rogers DC, Costall B, Domeney AM, Gerrard PA, Greener M, Kelly ME, Hagan JJ, Hunter AJ (2000) Anxiolytic profile of ropinirole in the rat, mouse and common marmoset. *Psychopharmacology (Berl)* 151: 91-97.
403. Eden RJ, Costall B, Domeney AM, Gerrard PA, Harvey CA, Kelly ME, Naylor RJ, Owen DA, Wright A (1991) Preclinical pharmacology of ropinirole (SK&F 101468-A) a novel dopamine D2 agonist. *Pharmacol Biochem Behav* 38: 147-154.
404. Baizman ER, Ezrin AM, Ferrari RA, Luttinger D (1987) Pharmacologic profile of fezolamine fumarate: a nontricyclic antidepressant in animal models. *J Pharmacol Exp Ther* 243: 40-54.
405. Bossert JM, Biskin RS, Franklin KB (2003) Systemic and intracerebroventricular administration of sodium barbital induced a place preference in rats. *Behav Pharmacol* 14: 517-523.

406. Chan TY (2009) Aconite poisoning. *Clin Toxicol (Phila)* 47: 279-285.
407. al AO, Bevan DR (1995) Clindamycin-induced neuromuscular blockade. *Can J Anaesth* 42: 614-617.
408. Gryniewicz G, Gadzikowska M (2008) Tropane alkaloids as medicinally useful natural products and their synthetic derivatives as new drugs. *Pharmacol Rep* 60: 439-463.
409. Makarovsky I, Markel G, Hoffman A, Schein O, Brosh-Nissimov T, Tashma Z, Dushnitsky T, Eisenkraft A (2008) Strychnine--a killer from the past. *Isr Med Assoc J* 10: 142-145.
410. Addicott MA, Marsh-Richard DM, Mathias CW, Dougherty DM (2007) The biphasic effects of alcohol: comparisons of subjective and objective measures of stimulation, sedation, and physical activity. *Alcohol Clin Exp Res* 31: 1883-1890.
411. Bainton RJ, Tsai LT, Singh CM, Moore MS, Neckameyer WS, Heberlein U (2000) Dopamine modulates acute responses to cocaine, nicotine and ethanol in *Drosophila*. *Curr Biol* 10: 187-194.
412. Phillips TJ, Shen EH (1996) Neurochemical bases of locomotion and ethanol stimulant effects. *Int Rev Neurobiol* 39: 243-282.
413. Correa M, Roig-Navarro AF, Aragon CM (2004) Motor behavior and brain enzymatic changes after acute lead intoxication on different strains of mice. *Life Sci* 74: 2009-2021.
414. Klee EW, Ebbert JO, Schneider H, Hurt RD, Ekker SC (2011) Zebrafish for the study of the biological effects of nicotine. *Nicotine Tob Res* 13: 301-312.
415. Ninkovic J, Bally-Cuif L (2006) The zebrafish as a model system for assessing the reinforcing properties of drugs of abuse. *Methods* 39: 262-274.