

Bibliografia di studio “Focal Brain Inflammation and Autism”

Articolo in lingua italiana: **“Autismo, Autoimmunità e Neuroinfiammazione”** -
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1. Theoharides TC, Zhang B, Conti P: Decreased mitochondrial function and increased brain inflammation in bipolar disorder and other neuropsychiatric diseases. *J Clin Psychopharmacol* 2011, 31:685–687.
2. Hagberg H, Gressens P, Mallard C: Inflammation during fetal and neonatal life: implications for neurologic and neuropsychiatric disease in children and adults. *Ann Neurol* 2012, 71:444–457.
3. Fombonne E: Epidemiology of pervasive developmental disorders. *Pediatr Res* 2009, 65:591–598.
4. Johnson CP, Myers SM: Identification and evaluation of children with autism spectrum disorders. *Pediatrics* 2007, 120:1183–1215.
5. McPartland J, Volkmar FR: Autism and related disorders. *Handb Clin Neurol* 2012, 106:407–418.
6. Abrahams BS, Geschwind DH: Advances in autism genetics: on the threshold of a new neurobiology. *Nat Rev Genet* 2008, 9:341–355.
7. Williams SC: Genetics: searching for answers. *Nature* 2012, 491:S4–S6.
8. Hornig M, Weissenbock H, Horscroft N, Lipkin WI: An infection-based model of neurodevelopmental damage. *Proc Natl Acad Sci USA* 1999, 96:12102–12107.
9. Hsiao EY, McBride SW, Chow J, Mazmanian SK, Patterson PH: Modeling an autism risk factor in mice leads to permanent immune dysregulation. *Proc Natl Acad Sci USA* 2012, 109:12776–12781.
10. Blenner S, Reddy A, Augustyn M: Diagnosis and management of autism in childhood. *BMJ* 2011, 343:d6238.
11. Rapin I, Tuchman RF: What is new in autism? *Curr Opin Neurol* 2008, 21:143–149.
12. Deth R, Muratore C, Benzecry J, Power-Charnitsky VA, Waly M: How environmental and genetic factors combine to cause autism: a redox/ methylation hypothesis. *Neurotoxicology* 2008, 29:190–201.

13. Lanni KE, Schupp CW, Simon D, Corbett BA: Verbal ability, social stress, and anxiety in children with autistic disorder. *Autism* 2012, 16:123–138.
14. Herbert MR: Contributions of the environment and environmentally vulnerable physiology to autism spectrum disorders. *Curr Opin Neurol* 2010, 23:103–110.
15. Goines PE, Ashwood P: Cytokine dysregulation in autism spectrum disorders (ASD): Possible role of the environment. *Neurotoxicol Teratol* 2012. doi:10.1016/j.ntt.2012.07.006.
16. Onore C, Careaga M, Ashwood P: The role of immune dysfunction in the pathophysiology of autism. *Brain Behav Immun* 2012, 26:383–392.
17. Theoharides TC, Angelidou A, Alysandratos KD, Zhang B, Asadi S, Francis K, Toniato E, Kalogeromitros D: Mast cell activation and autism. *Biochim Biophys Acta* 1822, 2012:34–41.
18. Theoharides TC, Alysandratos KD, Angelidou A, Delivanis DA, Sismanopoulos N, Zhang B, Asadi S, Vasiadi M, Weng Z, Miniati A, Kalogeromitros D: Mast cells and inflammation. *Biochim Biophys Acta* 1822, 2010:21–33.
19. Norrby K: Mast cells and de novo angiogenesis: angiogenic capability of individual mast-cell mediators such as histamine, TNF, IL-8 and bFGF. *Inflamm Res* 1997, 46(Suppl. 1):S7–S8.
20. Zhang B, Weng Z, Sismanopoulos N, Asadi S, Therianou A, Alysandratos KD, Angelidou A, Shirihai O, Theoharides TC: Mitochondria distinguish granule-stored from de novo synthesized tumor necrosis factor secretion in human mast cells. *Int Arch Allergy Immunol* 2012, 159(1):23–32.
21. Galli SJ: New concepts about the mast cell. *N Engl J Med* 1993, 328:257–265.
22. Theoharides TC, Doyle R: Autism, gut-blood–brain barrier and mast cells. *J Clin Psychopharm* 2008, 28:479–483.
23. Kim KS, Wass CA, Cross AS, Opal SM: Modulation of blood–brain barrier permeability by tumor necrosis factor and antibody to tumor necrosis factor in the rat. *Lymphokine Cytokine Res* 1992, 11:293–298.
24. Rossi CC, Van de Water J, Rogers SJ, Amaral DG: Detection of plasma autoantibodies to brain tissue in young children with and without autism spectrum disorders. *Brain Behav Immun* 2011, 25:1123–1135.
25. Braunschweig D, Ashwood P, Krakowiak P, Hertz-Picciotto I, Hansen R, Croen LA, Pessah IN, Van de Water J: Autism: maternally derived antibodies specific for fetal brain proteins. *Neurotoxicology* 2008, 29:226–231.
26. Braunschweig D, Duncanson P, Boyce R, Hansen R, Ashwood P, Pessah IN, Hertz-Picciotto I, Van de Water J: Behavioral correlates of maternal antibody status among children with autism. *J*

Autism Dev Disord 2012, 42(7):1435–1445.

27. Braunschweig D, Van de Water J: Maternal autoantibodies in autism. *Arch Neurol* 2012, 69:693–699.

28. Theoharides TC, Zhang B, Kempuraj D, Tagen M, Vasiadi M, Angelidou A, Alysandratos KD, Kalogeromitros D, Asadi S, Stavrianeas N, Peterson E, Leeman S, Conti P: IL-33 augments substance P-induced VEGF secretion from human mast cells and is increased in psoriatic skin. *Proc Natl Acad Sci USA* 2010, 107:4448–4453.

29. Moussion C, Ortega N, Girard JP: The IL-1-like cytokine IL-33 is constitutively expressed in the nucleus of endothelial cells and epithelial cells in vivo: a novel ‘alarmin’? *PLoS One* 2008, 3:e3331.

30. Enoksson M, Lyberg K, Moller-Westerberg C, Fallon PG, Nilsson G, Lunderius-Andersson C: Mast cells as sensors of cell injury through IL-33 recognition. *J Immunol* 2011, 186:2523–2528.

31. Zhao YY, Weir MA, Manno M, Cordy P, Gomes T, Hackam DG, Juurlink DN, Mamdani M, Moist L, Parikh CR, Paterson JM, Wald R, Yao Z, Garg AX: New fibrate use and acute renal outcomes in elderly adults: a population-based study. *Ann Intern Med* 2012, 156:560–569.

32. Pichery M, Mirey E, Mercier P, Lefrancais E, Dujardin A, Ortega N, Girard JP: Endogenous IL-33 is highly expressed in mouse epithelial barrier tissues, lymphoid organs, brain, embryos, and inflamed tissues: in situ analysis using a novel Il-33-LacZ gene trap reporter strain. *J Immunol* 2012, 188:3488–3495.

33. Chakraborty S, Kaushik DK, Gupta M, Basu A: Inflammasome signaling at the heart of central nervous system pathology. *J Neurosci Res* 2010, 88:1615–1631.

34. Donelan J, Boucher W, Papadopoulou N, Lytinas M, Papaliadis D, Theoharides TC: Corticotropin-releasing hormone induces skin vascular permeability through a neurotensin-dependent process. *Proc Natl Acad Sci USA* 2006, 103:7759–7764.

35. Theoharides TC, Konstantinidou A: Corticotropin-releasing hormone and the blood–brain-barrier. *Front Biosci* 2007, 12:1615–1628.

36. Vasiadi M, Therianou A, Alysandratos KD, Katsarou-Katsari A, Petrakopoulou T, Theoharides A, Papadavid E, Stavrianeas N, Antoniou C, Kalogeromitros D, Theoharides TC: Serum neurotensin (NT) is increased in psoriasis and NT induces VEGF release from human mast cells. *Br J Dermatol* 2012, 166:1349–1352.

37. Alysandratos K-D, Asadi S, Angelidou A, Zhang B, Sismanopoulos N, Yang H, Critchfield A, Theoharides TC: Neurotensin and CRH interactions augment human mast cell activation. *PLoS ONE* 2012, 7(11):e48934.

38. Asadi S, Theoharides TC: Corticotropin-releasing hormone and extracellular mitochondria augment IgE-stimulated human mast-cell vascular endothelial growth factor release, which is inhibited by luteolin. *J Neuroinflamm* 2012, 9:85.
39. Carraway R, Leeman SE: The isolation of a new hypotensive peptide, neurotensin, from bovine hypothalami. *J Biol Chem* 1973, 248:6854–6861.
40. Tyler-McMahon BM, Boules M, Richelson E: Neurotensin: peptide for the next millennium. *Regul Pept* 2000, 93:125–136.
41. Carraway RE, Singer EA, Ferris CF, Mitra SP: Generation of immunoreactive neurotensin(s) and enkephalin(s) by pepsin-treatment of plasma. *Adv Exp Med Biol* 1986, 198 Pt B:169–179.
42. Singh LK, Pang X, Alexacos N, Letourneau R, Theoharides TC: Acute immobilization stress triggers skin mast cell degranulation via corticotropin-releasing hormone, neurotensin and substance P: a link to neurogenic skin disorders. *Brain Behav Immunity* 1999, 13:225–239.
43. Carraway R, Cochrane DE, Lansman JB, Leeman SE, Paterson BM, Welch HJ: Neurotensin stimulates exocytotic histamine secretion from rat mast cells and elevates plasma histamine levels. *J Physiol* 1982, 323:403–414.
44. Feldberg RS, Cochrane DE, Carraway RE, Brown EB, Sawyer R, Hartunian M, Wentworth D: Evidence for a neurotensin receptor in rat serosal mast cells. *Inflamm Res* 1998, 47:245–250.
45. Barrocas AM, Cochrane DE, Carraway RE, Feldberg RS: Neurotensin stimulation of mast cell secretion is receptor-mediated, pertussis-toxin sensitive and requires activation of phospholipase C. *Immunopharmacology* 1999, 41:131–137.
46. Cochrane DE, Carraway RE, Boucher W, Feldberg RS: Rapid degradation of neurotensin by stimulated rat mast cells. *Peptides* 1991, 12:1187–1194.
47. Kalesnikoff J, Galli SJ: New developments in mast cell biology. *Nat Immunol* 2008, 9:1215–1223.
48. Kobayashi H, Ishizuka T, Okayama Y: Human mast cells and basophils as sources of cytokines. *Clin Exp Allergy* 2000, 30:1205–1212.
49. Galli SJ, Grimaldeston M, Tsai M: Immunomodulatory mast cells: negative, as well as positive, regulators of immunity. *Nat Rev Immunol* 2008, 8:478–486.
50. Kawakami T: A crucial door to the mast cell mystery knocked in. *J Immunol* 2009, 183:6861–6862.

51. Piconese S, Costanza M, Musio S, Tripodo C, Poliani PL, Gri G, Burocchi A, Pittoni P, Gorzanelli A, Colombo MP, Pedotti R: Exacerbated experimental autoimmune encephalomyelitis in mast-cell-deficient Kit W-sh/W-sh mice. *Lab Invest* 2011, 91:627–641.
52. Kogan MD, Blumberg SJ, Schieve LA, Boyle CA, Perrin JM, Ghandour RM, Singh GK, Strickland BB, Trevathan E, van Dyck PC: Prevalence of parent-reported diagnosis of autism spectrum disorder among children in the US, 2007. *Pediatrics* 2009, 5:1395–1403.
53. Angelidou A, Alysandratos KD, Asadi S, Zhang B, Francis K, Vasiadi M, Kalogeromitros D, Theoharides TC: Brief report: “allergic symptoms” in children with autism spectrum disorders. More than meets the eye? *J Autism Dev Disord* 2011, 41:1579–1585.
54. Pang X, Letourneau R, Rozniecki JJ, Wang L, Theoharides TC: Definitive characterization of rat hypothalamic mast cells. *Neuroscience* 1996, 73:889–902.
55. Fassio A, Evans G, Grisshammer R, Bolam JP, Mimmack M, Emson PC: Distribution of the neurotensin receptor NTS1 in the rat CNS studied using an amino-terminal directed antibody. *Neuropharmacology* 2000, 39:1430–1442.
56. Walker ME, Hatfield JK, Brown MA: New insights into the role of mast cells in autoimmunity: evidence for a common mechanism of action? *Biochim Biophys Acta* 1822, 2012:57–65.
57. Skaper SD, Giusti P, Facci L: Microglia and mast cells: two tracks on the road to neuroinflammation. *FASEB J* 2012, 26:3103–3117.
58. Skaper SD, Facci L: Mast cell-glia axis in neuroinflammation and therapeutic potential of the anandamide congener palmitoylethanolamide. *Philos Trans R Soc Lond B Biol Sci* 2012, 367:3312–3325.
59. Nagai A, Nakagawa E, Hatori K, Choi HB, McLarnon JG, Lee MA, Kim SU: Generation and characterization of immortalized human microglial cell lines: expression of cytokines and chemokines. *Neurobiol Dis* 2001, 8:1057–1068.
60. Morgan JT, Chana G, Abramson I, Semendeferi K, Courchesne E, Everall IP: Abnormal microglial-neuronal spatial organization in the dorsolateral prefrontal cortex in autism. *Brain Res* 2012, 1456:72–81.
61. Rodriguez JI, Kern JK: Evidence of microglial activation in autism and its possible role in brain underconnectivity. *Neuron Glia Biol* 2011, 7:205–213.
62. Martin S, Dicou E, Vincent JP, Mazella J: Neurotensin and the neurotensin receptor-3 in microglial cells. *J Neurosci Res* 2005, 81:322–326.

63. Riegler M, Castagliuolo I, Wang C, Wlk M, Sogukoglu T, Wenzl E, Matthews JB, Pothoulakis C: Neurotensin stimulates Cl(−) secretion in human colonic mucosa In vitro: role of adenosine. *Gastroenterology* 2000, 119:348–357.
64. Martin S, Vincent JP, Mazella J: Involvement of the neurotensin receptor-3 in the neurotensin-induced migration of human microglia. *J Neurosci* 2003, 23:1198–1205.
65. Ghanizadeh A: Targeting neurotensin as a potential novel approach for the treatment of autism. *J Neuroinflammation* 2010, 7:58.
66. Bear MF, Dolen G, Osterweil E, Nagarajan N: Fragile X: translation in action. *Neuropsychopharmacology* 2008, 33:84–87.
67. Michalon A, Sidorov M, Ballard TM, Ozmen L, Spooren W, Wettstein JG, Jaeschke G, Bear MF, Lindemann L: Chronic pharmacological mGlu5 inhibition corrects fragile X in adult mice. *Neuron* 2012, 74:49–56.
68. Rossignol DA, Frye RE: A review of research trends in physiological abnormalities in autism spectrum disorders: immune dysregulation, inflammation, oxidative stress, mitochondrial dysfunction and environmental toxicant exposures. *Mol Psychiatry* 2012, 17(4):389–401.
69. Rossignol DA, Frye RE: Mitochondrial dysfunction in autism spectrum disorders: a systematic review and meta-analysis. *Mol. Psychiatry* 2012, 17:290–314.
70. Zhang B, Angelidou A, Alysandratos KD, Vasiadi M, Francis K, Asadi S, Theoharides A, Sideri K, Lykouras L, Kalogeromitros D, Theoharides TC: Mitochondrial DNA and anti-mitochondrial antibodies in serum of autistic children. *J Neuroinflammation* 2010, 7:80.
71. Angelidou A, Francis K, Vasiadi M, Alysandratos K-D, Zhang B, Theoharides A, Lykouras L, Kalogeromitros D, Theoharides TC: Neurotensin is increased in serum of young children with autistic disorder. *J Neuroinflam* 2010, 7:48.
72. Zhang B, Alysandratos KD, Angelidou A, Asadi S, Sismanopoulos N, Delivanis DA, Weng Z, Miniati A, Vasiadi M, Katsarou-Katsari A, Miao B, Leeman SE, Kalogeromitros D, Theoharides TC: Human mast cell degranulation and preformed TNF secretion require mitochondrial translocation to exocytosis sites: relevance to atopic dermatitis. *J Allergy Clin Immunol* 2011, 127:1522–1531.
73. Zhang B, Asadi S, Weng Z, Sismanopoulos N, Theoharides TC: Stimulated human mast cells secrete mitochondrial components that have autocrine and paracrine inflammatory actions. *PLoS ONE* 2012, 7(12):e49767.
74. Lauritzen KH, Moldestad O, Eide L, Carlsen H, Nesse G, Storm JF, Mansuy IM, Bergersen LH, Klungland A: Mitochondrial DNA toxicity in forebrain neurons causes apoptosis, neurodegeneration, and impaired behavior. *Mol Cell Biol* 2010, 30:1357–1367.

75. Angelidou A, Asadi S, Alysandratos KD, Karagkouni A, Kourembanas S, Theoharides TC: Perinatal stress, brain inflammation and risk of autism-Review and proposal. *BMC Pediatr* 2012, 12:89.
76. Theoharides TC, Kempuraj D, Redwood L: Autism: an emerging 'neuroimmune disorder' in search of therapy. *Exp Opin Pharmacother* 2009, 10:2127–2143.
77. Aldinger KA, Plummer JT, Qiu S, Levitt P: SnapShot: genetics of autism. *Neuron* 2011, 72:418.
78. Betancur C: Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting. *Brain Res* 2011, 1380:42–77.
79. Zhou J, Parada LF: PTEN signaling in autism spectrum disorders. *Curr Opin Neurobiol* 2012, 22(5):873–879.
80. Smrz D, Kim MS, Zhang S, Mock BA, Smrzova S, DuBois W, Simakova O, Maric I, Wilson TM, Metcalfe DD, Gilfillan AM: mTORC1 and mTORC2 differentially regulate homeostasis of neoplastic and non-neoplastic human mast cells. *Blood* 2011, 118:6803–6813.
81. Shang YC, Chong ZZ, Wang S, Maiese K: Erythropoietin and Wnt1 govern pathways of mTOR, Apaf-1, and XIAP in inflammatory microglia. *Curr Neurovasc Res* 2011, 8:270–285.
82. Weiss LA, Arking DE, Daly MJ, Chakravarti A: A genome-wide linkage and association scan reveals novel loci for autism. *Nature* 2009, 461:802–808.
83. Gerhard T, Chavez B, Olfson M, Crystal S: National patterns in the outpatient pharmacological management of children and adolescents with autism spectrum disorder. *J Clin Psychopharmacol* 2009, 29:307–310.
84. Lang R, Mahoney R, El Zein F, Delaune E, Amidon M: Evidence to practice: treatment of anxiety in individuals with autism spectrum disorders. *Neuropsychiatr Dis Treat* 2011, 7:27–30.
85. Warren Z, McPheeters ML, Sathe N, Foss-Feig JH, Glasser A, Veenstra-Vanderweele J: A systematic review of early intensive intervention for autism spectrum disorders. *Pediatrics* 2011, 127:e1303–e1311.
86. Munshi KR, Gonzalez-Heydrich J, Augenstein T, D'Angelo EJ: Evidence- based treatment approach to autism spectrum disorders. *Pediatr Ann* 2011, 40:569–574.
87. Nazeer A: Psychopharmacology of autistic spectrum disorders in children and adolescents. *Pediatr Clin North Am* 2011, 58:85–97.

88. Parikh MS, Kolevzon A, Hollander E: Psychopharmacology of aggression in children and adolescents with autism: a critical review of efficacy and tolerability. *J Child Adolesc Psychopharmacol* 2008, 18:157–178.
89. Posey DJ, Stigler KA, Erickson CA, McDougle CJ: Antipsychotics in the treatment of autism. *J Clin Invest* 2008, 118:6–14.
90. Chavez B, Chavez-Brown M, Sopko MA Jr, Rey JA: Atypical antipsychotics in children with pervasive developmental disorders. *Paediatr Drugs* 2007, 9:249–266.
91. McDougle CJ, Stigler KA, Erickson CA, Posey DJ: Atypical antipsychotics in children and adolescents with autistic and other pervasive developmental disorders. *J Clin Psychiatry* 2008, 69(Suppl 4):15–20.
92. McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, Arnold LE, Lindsay R, Nash P, Hollway J, McDougle CJ, Posey D, Swiezy N, Kohn A, Scahill L, Martin A, Koenig K, Volkmar F, Carroll D, Lancor A, Tierney E, Ghuman J, Gonzalez NM, Grados M, Vitiello B, Ritz L, Davies M, Robinson J, McMahon D: Risperidone in children with autism and serious behavioral problems. *N Engl J Med* 2002, 347:314–321.
93. Scott LJ, Dhillon S: Risperidone: a review of its use in the treatment of irritability associated with autistic disorder in children and adolescents. *Paediatr Drugs* 2007, 9:343–354.
94. Curran MP: Aripiprazole: in the treatment of irritability associated with autistic disorder in pediatric patients. *Paediatr Drugs* 2011, 13:197–204.
95. Research Units on Pediatric Psychopharmacology Autism Network: Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Arch Gen Psychiatry* 2005, 62:1266–1274.
96. McPheeters ML, Warren Z, Sathe N, Bruzek JL, Krishnaswami S, Jerome RN, Veenstra-Vanderweele J: A systematic review of medical treatments for children with autism spectrum disorders. *Pediatrics* 2011, 127:e1312–e1321.
97. Williams K, Wheeler DM, Silove N, Hazell P: Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorders (ASD). *Cochrane Database Syst Rev* 2010, 8, CD004677.
98. King BH, Hollander E, Sikich L, McCracken JT, Scahill L, Bregman JD, Donnelly CL, Anagnostou E, Dukes K, Sullivan L, Hirtz D, Wagner A, Ritz L: Lack of efficacy of citalopram in children with autism spectrum disorders and high levels of repetitive behavior: citalopram ineffective in children with autism. *Arch Gen Psychiatry* 2009, 66:583–590.
99. Volkmar FR: Citalopram treatment in children with autism spectrum disorders and high levels of repetitive behavior. *Arch Gen Psychiatry* 2009, 66:581–582.

100. Correll CU, Kratochvil CJ, March JS: Developments in pediatric psychopharmacology: focus on stimulants, antidepressants, and antipsychotics. *J Clin Psychiatry* 2011, 72:655–670.
101. Zhou H, Luo Y, Huang S: Updates of mTOR inhibitors. *Anticancer Agents Med Chem* 2010, 10:571–581.
102. Ehninger D, Silva AJ: Rapamycin for treating Tuberous sclerosis and Autism spectrum disorders. *Trends Mol Med* 2011, 17:78–87.
103. Sahin M: Targeted treatment trials for tuberous sclerosis and autism: no longer a dream. *Curr Opin Neurobiol* 2012, 22(5):895–901.
104. de Vries PJ: Targeted treatments for cognitive and neurodevelopmental disorders in tuberous sclerosis complex. *Neurotherapeutics*. 2010, 7:275–282.
105. Hampson DR, Gholizadeh S, Pacey LK: Pathways to drug development for autism spectrum disorders. *Clin Pharmacol Ther* 2012, 91:189–200.
106. Middleton E Jr, Kandaswami C, Theoharides TC: The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease and cancer. *Pharmacol Rev* 2000, 52:673–751.
107. Van Aller GS, Carson JD, Tang W, Peng H, Zhao L, Copeland RA, Tummino PJ, Luo L: Epigallocatechin gallate (EGCG), a major component of green tea, is a dual phosphoinositide-3-kinase/mTOR inhibitor. *Biochem Biophys Res Commun* 2011, 406:194–199.
108. Kimata M, Shichijo M, Miura T, Serizawa I, Inagaki N, Nagai H: Effects of luteolin, quercetin and baicalein on immunoglobulin E-mediated mediator release from human cultured mast cells. *Clin Exp Allergy* 2000, 30:501–508.
109. Asadi S, Zhang B, Weng Z, Angelidou A, Kempuraj D, Alysandratos KD, Theoharides TC: Luteolin and thiosalicylate inhibit HgCl₂ and thimerosal-induced VEGF release from human mast cells. *Int J Immunopathol Pharmacol* 2010, 23:1015–1020.
110. Dirscherl K, Karlstetter M, Ebert S, Kraus D, Hlawatsch J, Walczak Y, Moehle C, Fuchshofer R, Langmann T: Luteolin triggers global changes in the microglial transcriptome leading to a unique anti-inflammatory and neuroprotective phenotype. *J Neuroinflammation* 2010, 7:3.
111. Jang S, Dilger RN, Johnson RW: Luteolin inhibits microglia and alters hippocampal-dependent spatial working memory in aged mice. *J Nutr* 2010, 140:1892–1898.
112. Kao TK, Ou YC, Lin SY, Pan HC, Song PJ, Raung SL, Lai CY, Liao SL, Lu HC, Chen CJ: Luteolin inhibits cytokine expression in endotoxin/cytokine-stimulated microglia. *J Nutr Biochem* 2011, 22:612–624.

113. Kempuraj D, Tagen M, Iliopoulou BP, Clemons A, Vasiadi M, Boucher W, House M, Wolfberg A, Theoharides TC: Luteolin inhibits myelin basic protein-induced human mast cell activation and mast cell dependent stimulation of Jurkat T cells. *Br J Pharmacol* 2008, 155:1076–1084.
114. Verbeek R, Plomp AC, van Tol EA, van Noort JM: The flavones luteolin and apigenin inhibit in vitro antigen-specific proliferation and interferon- γ production by murine and human autoimmune T cells. *Biochem Pharmacol* 2004, 68:621–629.
115. Franco JL, Posser T, Missau F, Pizzolatti MG, Dos Santos AR, Souza DO, Aschner M, Rocha JB, Dafre AL, Farina M: Structure-activity relationship of flavonoids derived from medicinal plants in preventing methylmercury- induced mitochondrial dysfunction. *Environ Toxicol Pharmacol* 2010, 30:272–278.
116. Chen HQ, Jin ZY, Wang XJ, Xu XM, Deng L, Zhao JW: Luteolin protects dopaminergic neurons from inflammation-induced injury through inhibition of microglial activation. *Neurosci Lett* 2008, 448:175–179.
117. Jang SW, Liu X, Yepes M, Shepherd KR, Miller GW, Liu Y, Wilson WD, Xiao G, Blanche B, Sun YE, Ye K: A selective TrkB agonist with potent neurotrophic activities by 7,8-dihydroxyflavone. *Proc Natl Acad Sci USA* 2010, 107:2687–2692.
118. Sadakata T, Shinoda Y, Oka M, Sekine Y, Sato Y, Saruta C, Miwa H, Tanaka M, Itohara S, Furuichi T: Reduced axonal localization of a Caps2 splice variant impairs axonal release of BDNF and causes autistic-like behavior in mice. *Proc Natl Acad Sci USA* 2012, 109(51):21104–21109.
119. Theoharides TC, Asadi S, Panagiotidou S: A case series of a luteolin formulation (NeuroprotekW) in children with autism spectrum disorders. *Intl J Immunopathol Pharmacol* 2012, 25:317–323.