

B. 1990
(11)

UNIVERSIDAD DE BUENOS AIRES
FACULTAD DE CIENCIAS EXACTAS Y NATURALES ;

Departamento de Ciencias Biologicas

Asignatura: PROBLEMAS ABIERTOS EN NEUROBIOLOGIA

Carrera: Ciencias Biologicas

Caracter: Posgrado

Horas de clase 21 ; Seminarios: 21 ; Total: 42 horas

4
DR. FERNANDO O. KRAVETZ
DIRECTOR (I)
Dpto. CIENCIAS BIOLOGICAS

M

CP452/90

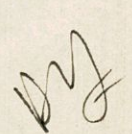
CURSO DE POSGRADO
Daniel J. Goldstein
PROBLEMAS ABIERTOS EN NEUROBIOLOGIA

1

Neuronas y glia: anatomia, fisiologia, farmacologia y bioquimica. Interaccion entre neuronas y glia. Neurotransmision. Biosintesis de transmisores. El perfil macromolecular de la neurotransmision. Fosforilacion de proteinas y modulacion de la biosintesis de transmisores. Modulacion de la expresion de los peptidos neurotransmisores. Neurotransmision como señalizacion autocrina y paracrina. Unidad bioquimica y funcional de los sistemas quimicos de comunicacion. Plasticidad bioquimica y plasticidad estructural en neurobiologia. Receptores. Los canales como proteinas: analisis de las estructuras moleculares de los canales activados por voltaje, por ligandos, y los receptores acoplados a proteinas ligadoras de guanil-nucleotidos. Tecnicas bioquimicas e histoquimicas para el estudio de receptores. Analogos agonistas y analogos antagonistas. Historia y evolucion de la estrategia de busqueda de agentes farmacologicos. Farmacologia, bioquimica, y biologia molecular de receptores. Receptores y canales ionicos. La transduccion de la senales. Segundos mensajeros. Regulacion fisiologica y farmacologica de la transduccion. Analisis de los problemas abiertos en el estudio de los receptores beta-adrenergico, colinergicos nicotinicos y muscarinicos, GABA, histaminergicos, serotoninergicos, y encefalinergicos.

2

La neurona como celula. El problema general de "homing" en biologia. La neurona como celula endocrina, paracrina y autocrina. Fisiologia, bioquimica y biologia molecular de la especificidad topografica y migratoria neuronal. Mecanismo de crecimiento y direccionalidad axonica. Los factores troficos. Diferenciacion neuronal y glial. La biologia molecular de la membrana neuronal. Fascilina II. Analisis genetico, bioquimico y molecular de la superfamilia de las inmunoglobulinas de membrana. Analogias y diferencias entre los mecanismos de reconocimiento y


DR. FERNANDO O. KRAVETZ
DIRECTOR (II)
Dpto. CIENCIAS BIOLÓGICAS

respuesta entre los sistemas inmune y neuronal. La biología molecular del citoesqueleto neuronal y el crecimiento axónico.

3

Los modelos actuales de la neurobiología: sus ventajas y sus inconvenientes. Gusanos, moscas, sanguijuelas, caracoles, bacterias, ~~una~~ ratones y seres humanos. La importancia de los animales transgénicos para la producción de modelos experimentales rigurosos y útiles. Similitudes y diferencias entre el sistema inmune y el sistema nervioso. Moléculas comunes, estrategias comunes, problemas comunes. La "genética reversa" y la neurobiología. Modelos humanos para el estudio del crecimiento, la diferenciación, y la muerte neuronal: Alzheimer, Huntington, von Recklinghausen (tipos I y II), kuru-kuru, teosaurismosis y neoplasias. El control de la proliferación neuronal.

BIBLIOGRAFIA

- Allen, N.D., Cran, D.G., Barton, S.C., Hettle, S., Reik, W. & Surami, M.A. Transgenes as probes for active chromosomal domains in mouse development. Nature 333: 852-855 (1988).
- Allende, J.E. GTP-mediate macromolecular interactions: the common features of different systems. FASEB Journal 2: 2356-2367 (1988).
- Andersen, A.S. Cell biology: reception and transmission. Nature 337:12 (1989).
- Antonarakis, S.E. Diagnosis of genetic disorders at the DNA level. New England Journal of Medicine 320: 153-170 (1989).
- Agnew, W.S. Excitation-contraction coupling: proteins that bridge the gap. Nature 334: 299-300 (1988).
- Alarcon, B., Regueiro, J.R., Arnaiz-Villena, A. & Terhorst, C. Familial defect in the surface expression of the T-cell receptor-CD3 complex. New England Journal of Medicine 319: 1203-1208 (1988).
- Bajorath, J., Raghunathan, S., Hinrichs, W. & Saenger, W. Long-range structural changes in proteinase K triggered by calcium ion removal. Nature 337:481-484 (1989).
- A X Bevilacqua, M.P., Stengelin, S., Gimbrone, M.A. & Seed, B. Endothelial leukocyte adhesion molecule 1: an inducible receptor for neutrophils related to complement regulatory proteins and lectins. Science 243: 1160-1165.

DR. FERNANDO O. KRAVETZ
DIRECTOR (I)
DTG. CIENCIAS BIOLÓGICAS

- Blackshear, P.J., Nairn, A.C. & Kuo, J.F. Protein kinases 1988: a current perspective. FASEB Journal 2: 2957-2969 (1988).
- Bourne, H.R. G-protein subunits: who carries what message? Nature 337: 404-405 (1989).
- Brenner, S. The molecular evolution of genes and proteins: a tale of two serines. Nature 334: 528-530 (1988).
- Broadus, A.E., Mangin, Ikeda, K., Insogna, K.I., Weir, E.C., Burtis, W.J. & Steart, A.F. Humoral hypercalcemia of cancer: identification of a novel parathyroid hormone like-peptide. New England Journal of Medicine 319: 556-563 (1988).
- Brodsky, F.M. Living with clathrin: its role in intracellular membrane traffic. Science 242: 1396-1402 (1988).
- Carmel, R., Lau, K.H.W., Baylink, D.J., Saxcena, S. & Singer, F.R. Cobalamin and osteoblast-specific proteins. New England Journal of Medicine 318: 70-75 (1988).
- Catterall, W.A. Structure and function of voltage-sensitive ion channels. Science 242: 50-61 (1988).
- Chinkers, M., Garbers, D.L., Chang, M.S., Lowe, D.G., Chin, H., Goeddel, D.L. & Schulz, S. A membrane form of guanylate cyclase is an atrial natriuretic peptide receptor. Nature 338: 78-83 (1989).
- Colquhoun, D. A new type of ion-channel block. Nature 329: 204-205 (1987).
- Cooke, H.J. Role of the "little brain" in the gut in water and electrolyte homeostasis. FASEB Journal 3: 127-138 (1989).
- Crabtree, G.R. Contingent genetic regulatory events in T lymphocyte activation. Science 243: 355-361 (1989).
- Crick, F.H.C. The recent excitement about neural networks. Nature 337: 129-132 (1989).
- Davis, M.M. & Bjorkman, P.J. T-cell antigen receptor genes and T-cell recognition. Nature 334: 395-402 (1988).
- de Vrije, T., de Swart, R.L., Dowhan, W., Tommassen, J. & de Kruijff, B. Phosphatidylglycerol is involved in protein translocation across Escherichia coli inner membranes. Nature 334: 173-175 (1988).
- Dodd, J. & Jessell, T.M. Axon guidance and the patterning of neuronal projections in vertebrates. Science 242: 692-699 (1988).

up

DR. FERNANDO C. KRAYCH

DIRECTOR

DETO. CIENCIAS BIOLÓGICAS

- Erdoş, E.G. & Skidgel, R.A. Neutral endopeptidase 24:11 (enkephalinase) and related regulators of peptide hormones. FASEB Journal 3: 145-151 (1989).
- Exton, J.H. Mechanisms of action of calcium-mobilizing agonists: some variations on a young theme. FASEB Journal 2: 2670-2676 (1988).
- Falke, J.J. & Koshland Jr, D.E. Global flexibility in a sensory receptor: a site-directed cross-linking approach. Science 237: 1596-1600 (1987).
- Founder, J.W., Pearce, P.T., Smith, R. & Smith, A.I. Mineralocorticoid action: target tissue specificity is enzyme, not receptor, mediated. Science 242: 583-585 (1988).
- Hanks, S.K., Quinn, A.M. & Hunter, T. The protein kinase family: conserved features and deduced phylogeny of the catalytic domains. Science 241: 42-52 (1988).
- Hanley, M.R. & Jackson, T. Substance K receptor: return of the magnificent seven. Nature 329: 766-767 (1987).
- Hemmings, H.C., Nairn, A.C., McGuinness, T.L., Huganir, R.L. & Greengard, P. Role of protein phosphorylation in neuronal signal transduction. FASEB Journal 3: 1583-1592 (1989).
- Hess, J.F., Bourret, R.B. & Simon, M.I. Histidine phosphorylation and phosphoryl transfer in bacterial chemotaxis. 336: 139-143 (1988).
- Hirschowitz, B.I., Hammer, R., Giachetti, A., Keirns, J.J. & Levine, R.R. Subtypes of muscarinic receptors. TIPS, Elsevier (1984)
- A * Harrelson, A.L. & Goodman, C.S. Growth cone guidance in insects: fascilin II is a member of the immunoglobulin superfamily. Science 242: 700-708 (1988).
- Hunter, D.D., Shah, V., Merlie, J.P. & Sanes, J.R. A laminin-like adhesive protein concentrated in the synaptic cleft of the neuromuscular junction. Nature 338:229-234 (1989).
- Imoto, K., Busch, C., Sakmann, B., Mishina, M., Konno, T., Nakai, J., Bujo, H., Mori, Y., Fukuda, K. & Numa, S. Nature 335: 645-648 (1988).
- Jackson, T.R., Blair, L.A.C., Marshall, J., Goedert, M. & Hanley, M.R. The mas oncogene encodes an angiotensin receptor. Nature 335: 437-440 (1988).

- Janeway, C.A. Molecular recognition: frontiers of the immune system. Nature 333: 804-805 (1988),
- Jacob, R., Merritt, J.E., Hallam, T.J. & Rink, T.J. Repetitive spikes in cytoplasmic calcium evoked by histamine in human endothelial cells. Nature 335: 40-45 (1988).
- B * Kennedy, M.R. Cellular neurobiology: synaptic memory molecules. Nature 335: 770-771 (1988).
- Kothary, R., Clapoff, S., Brown, A., Campbell, R., Peterson, A. & Rossant, J. A transgene containing lacZ inseted in dystonia locus is expressed in neural tube. Nature 438-437 (1988).
- Knapp, R.J., Kazmierski, W., Hruby, V.J. & Yamamura, H.I. Structural characteristics of two highly selective opioid peptides. BioEssays 10: 58-61 (1989).
- Limbird, L.E. Receptors linked to inhibition of adenylate cyclase: additional signaling mechanisms. FASEB Journal 2: 2686-2695 (1988).
- Leonard, R.J., Labarca, C.G., Charnet, P., Davidson, N. & Lester, H.A. Evidence that the M2 membrane-spanning region lines the ion channel pore of the nicotinic receptor. Science 242: 1578-1581 (1988).
- Levitzki, A. From epinephrine to cyclic AMP. Science 241: 800-806 (1988).
- Lester, H.A. Heterologous expression of excitability proteins: route to more specific drugs? Science 1057-1063 (1988).
- Lindenbaum, J., Healton, E.B., Savage, D.G., Brust, J.C.M., Garrett, T.J., Podell, E.R., Marcell, P.D., Stabler, S.P. & Allen, R.P. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. New England Journal of Medicine 318: 1720-1728 (1988).
- Low, M.G. Glycosyl-phosphatidylinositol: a versatile anchor for cell surface proteins. FASEB Journal 3: 1600-1608 (1989).
- McCune, J.M., Namikawa, R., Kaneshima, H., Shultz, L.D., Lieberman, M. & Weissman, I.L. The SCID-hu mouse: murine model for the analysis of human hematolymphoid differentiation and function. Science 241: 1632-1639 (1988).
- Miele, L., Cordella-Miele, E., Facchiano, A. & Mukherjee, A.B. Novel anti-inflammatory peptides from the region of highest

similarity between uteroglobin and lipocortin I. Nature 335: 726-730 (1988).

A Nakache, M., Berg, E.L., Streeter, P.R. & Butcher, E.C. The mucosal vascular adhesion molecule is a tissue-specific endothelial cell adhesion molecule for circulating lymphocytes. Nature 337: 179-181 (1989).

Neer, E.J. & Clapham, D.E. Roles of G protein subunits in transmembrane signaling. Nature 333: 129-134 (1988).

Nishizuka, Y. The molecular heterogeneity of protein kinase C and its implications for cellular regulation. Nature 334: 661-665 (1988).

Nudel, U., Zuk, D., Einat, P., Zeelon, E., Levy, Z., Neuman, S. & Jaffe, D. Duchenne muscular dystrophy gene product is not identical in muscle and brain. Nature 337: 76-78 (1989).

Paigen, K. Gene regulation and its role in evolutionary processes. In Evolutionary Processes and Theory, Academic Press (1986).

Palmert, M.R., Golde, T.E., Cohen, M.L., Kovacs, D.M., Tanzi, R.E., Gusella, J.F., Usiak, M.F., Younkin, L.H. & Youkin, S.G. Amyloid protein precursor messenger RNAs: differential expression in Alzheimer's disease. Science 241: 1080-1083 (1988).

Peralta, E.G., Ashkenazi, A., Winslow, J.W., Ramachandran, J. & Capon, D.J. Differential regulation of PI hydrolysis and adenylcyclase by muscarinic receptor subtypes. Nature 334: 434-437 (1988).

Pearson, R.B., Wettenhall, R.E.H., Means, A.R., Hartshorne, D.J. & Kemp, B.E. Autoregulation of enzymes by pseudosubstrate prototopes: myosin light-chain kinase. Science 241: 970-973 (1988).

Platt, J.R. Strong inference. Science 146: 347-353 (1964).

Purves, D., Snider, W.D. & Voydovic, J.T. Trophic regulation of nerve cell morphology and innervation in the autonomic nervous system. Nature 336: 123-128 (1988).

Ramachandran, J., Peralta, E.G., Ashkenazi, A., Winslow, J.W. & Capon, D.J. The structural and functional interrelationships of muscarinic acetylcholine receptor subtypes. BioEssays 10: 54-57 (1989).

DR. FERNANDO O. KRAVETZ
DIRECTOR (I)
Dpto. CIENCIAS BIOLÓGICAS

Raff, M.C. Glial cell diversification in the rat optic nerve. Science 243: 1450-1455 (1989).

Rosenblatt, M. Peptide hormone antagonists that are effective in vivo. New England Journal of Medicine 315: 1004-1013 (1986).

Rubin, H. Molecular biology running into a cul-de-sac? Nature 335: 121 (1988).

Ryan, R.J., Charlesworth, M.C., McCromick, D.J., Milius, R.P. & Keutmann, H.T. The glycoprotein hormones: recent studies of structure-function relationships. FASEB Journal 2: 2661-2669 (1988).

Saier, M.H., Yamada, M., Erni, B., Suda, K., Lengeler, J., Ebner, R., Argos, P., Rak, B. Schnetz, K., Lee, C.A., Stewart, G.C., Breidt, F., Waygood, E.B., Peri, K.G. & Doolittle, R.F. Sugar permeases of the bacterial phosphoenolpyruvate-dependent phosphotransference system: sequence comparisons. FASEB Journal 2: 199-298 (1988).

Saleme, F.R. Structural polymorphism in transmembrane channels. Science 241:145-146 (1988).

Saxena, S.P., Brandes, L.J., Becker, A.B., Simons, K.J., LaBella, F.S. & Gerrard, J.M. Histamine is an intracellular messenger mediating platelet aggregation. Science 243: 1596-1599 (1989).

Selvaraj, P., Rosse, W.F., Silber, R. & Springer, W.F. The major Fc receptor has a phosphatidylinositol anchor and is deficient in paroxysmal nocturnal hemoglobinuria. Nature 333: 565-567 (1988).

Scherrer, P., McGinnis, K. & Bogomolni, R.A. Biochemical and spectroscopic characterization of the blue-green photoreceptor in *Halobacterium halobium*. Proceedings of the National Academy of Sciences USA 84: 402-406 (1987).

Shinkai, Y., Takio, K. & Okumura, K. Homology of perforin to the ninth component of complement (C9). Nature 334:525-527 (1988).

Siegelman, M.H., van de Rijn, M. & Weissman, I.L. Mouse lymph node homing receptor cDNA clone encodes a glycoprotein revealing tandem interaction domains. Science 243: 1165-1172 (1989).

Sims, J.E., March, C.J., Cosman, D., Widmer, M.B., MacDonald, H.R., McMahan, C.J., Grubin, C.E., Wignall, J.M., Jackson, J.L.,

B + Call, S.M., Friend, D., Alpert, A.R., Gillis, S., Urdal, D.L. & Dower, S.K. cDNA expression cloning of the IL-1 receptor, a

member of the immunoglobulin superfamily. Science 241: 585-589 (1988).

Shenolikar, S. Protein phosphorylation: hormones, drugs, and bioregulation. FASEB Journal 2:2753-2764 (1988).

Schotzinger, R.J. & Landis, S.C. Cholinergic phenotype developed by noradrenergic sympathetic neurons after innervation of a novel cholinergic target in vivo. Nature 335:637-640.

Silva, A.M., Cachau, R.E. & Goldstein, D.J. Ion channels in southern bean mosaic virus. Biophysical Journal 52: 595-602 (1987).

Simmons, D. & Seed, B. The Fc gamma receptor of natural killer cells is a phospholipid-linked membrane protein. Nature 333: 568-570 (1988).

Smith, S.J. Neuronal cytom mechanics: the actin-based motility of growth cones. Science 242: 708-714.

Sprang, S.R., Acharya, K.R., Goldsmith, E.J., Stuart, D.I., Varvill, K., Fletterick, R.J., Madsen, N.B. & Johnson, L.N. Structural changes in glycogen phosphorylase induced by phosphorylation. Nature 336: 215-221 (1988).

Spudich, J.L. & Bogomolni, R.A. Mechanism of colour discrimination by a bacterial sensory rhodopsin. Nature 312: 509-513 (1984).

Stoeckenius, W. & Bogomolli, R.A. Bacteriorhodopsin and related pigments of halobacteria. Annual Review of Biochemistry 52: 587-616 (1982).

Stornetta, R.L., Hawelu-Johnson, C.L., Guyenet, P.G. & Lynch, K.R. Astrocytes synthesize angiotensinogen in brain. Science 242: 1444-1446 (1988).

Tanabe, T., Beam, K.G., Powell, J.A. & Numa, S. Restoration of excitation-contraction coupling and slow calcium current in dysgenic muscle by dihydropyridine receptor complementary DNA. Nature 336: 134-139 (1988).

Taylor, J.W. & Kaiser, E.T. The structural characterization of beta-endorphin and related peptide hormones and neurotransmitters. Pharmacological Reviews 38: 291-319 (1986).

Taylor, S.S., Bubis, J., Toner-Webb, J., Saraswat, L.D., First, E.A., Buechler, J.A., Knighton, D.R. & Sowadski, J. AMP-dependent protein kinase: prototype of a family of enzymes. FASEB Journal 2: 2677-2685 (1988).

DR. FERNANDO C. KRAVETZ
DIRECTOR (I)
Dpto. CIENCIAS BIOLÓGICAS

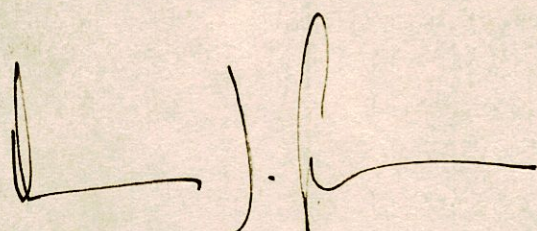
- B x Tigges, M.A., Casey, L.S. & Koshland, M.E. Mechanism of interleukin-2 signaling: mediation of different outcomes by a single receptor and transduction pathway. Science 243: 781-786 (1989).
- Vogel, J., Hinrichs, S.H., Reynolds, R.K., Luciw, P.A. & Jay, G. The HIV tat gene induces dermal lesions resembling Kaposi's sarcoma in transgenic mice. Nature 335: 606-617 (1988).
- Wallace, B.A. & Ravikumar, K. The gramicidin pore: crystal structure of a cesium complex. Science 241: 182-191 (1988).
- Waneck, G.L., Stein, M.E. & Flavell, R.A. Conversion of a PI-anchored protein to an integral membrane protein by a single amino acid mutation. Science 241: 697-700 (1988).
- Weiss, J.H. & Choi, D.W. Beta-N-methylamino-L-alanine neurotoxicity: requirement for bicarbonate as a cofactor. Science 241: 973-975 (1988).
- Weiss, E.R., Kelleher, D.J., Woon, C.W., Soparkar, S., Osawa, S., Heasley, L.E. & Johnson, G.L. Receptor activation of G proteins. FASEB Journal 2: 2841-2848 (1988).
- Wertelecki, W., Rouleau, G.A., Superneau, D.W., Forehand, L.W., Williams, J.P., Haines, J.L. & Gusella, J.F. Neurofibromatosis II: clinical and DNA linkage studies of a large kindred. New England Journal of Medicine 319: 278-283 (1988).
- Westphal, H. Transgenic mammals and biotechnology. FASEB Journal 3: 117-120 (1989).
- Williams, L.T. Signal transduction by the platelet-derived growth factor receptor. Science 243: 1564-1570 (1989).
- Wolff, E.K., Bogomolni, R.A., Scherrer, P., Hess, B. & Stoerkenius, W. Color discrimination in halobacteria: spectroscopic characterization of a second sensory receptor covering the blue-green region of the spectrum. Proceedings of the National Academy of Sciences USA 83: 7272-7276 (1986).
- Yancopoulos, G.D. & Alt, F.W. Reconstruction of an immune system. Science 241: 1581-1583 (1988).
- Yochem, J., Westo, K. & Greenwald, I. The *Caenorhabditis elegans* lin-12 gene encodes a transmembrane protein with overall similarity to *Drosophila* Notch. Nature 335: 5476-550 (1988).
- Yoshimasa, Y., Seino, S., Whittaker, J., Kakehi, T., Kosaki, A., Kusuya, H., Imura, H., Bell, G. & Steiner, D. Insulin-resistant

diabetes due to a point mutation that prevents insulin
prereceptor processing. Science 240:784-790 (1988).

Zuber, H. Structure of light-harvesting antenna complexes of
photosynthetic bacteria, cyanobacteria and red algae. TIBS 11:
414-419 (1986).

His secretary

Teowe



David J. Gwynne



BERNARD C. KRAVETZ
DIRECTOR (I)
CIENCIAS BIOLÓGICAS

