

## References

### Description

- Abbas, A. K., Lichtman, A. H., and Pillai, S. (2015) Cellular and Molecular Immunology. Elsevier.
- Adams, G. P., and Weiner, L. M. (2005) Monoclonal antibody therapy of cancer. *Nat Biotech* 23, 1147–1157.
- Alexander, J., del Guercio, M.-F., Maewal, A., Qiao, L., Fikes, J., Chesnut, R. W., Paulson, J., Bundle, D. R., DeFrees, S., and Sette, A. (2000) Linear PADRE T Helper Epitope and Carbohydrate B Cell Epitope Conjugates Induce Specific High Titer IgG Antibody Responses. *J. Immunol.* 164, 1625 LP-1633.
- Allen, J. R., Harris, C. R., and Danishefsky, S. J. (2001) Pursuit of Optimal Carbohydrate-Based Anticancer Vaccines : Preparation of a Multiantigenic Unimolecular Glycopeptide Containing the Tn, MBr1, and Lewisy Antigens. *J. Am. Chem. Soc.* 123, 1890–1897.
- Almeida, J. P. M., Figueroa, E. R., and Drezek, R. A. (2014) Gold nanoparticle mediated cancer immunotherapy. *Nanomedicine Nanotechnology, Biol. Med.* 10, 503–514.
- Ashizawa, T., Miyata, H., Ishii, H., Oshita, C., Matsuno, K., Masuda, Y., Furuya, T., Okawara, T., Otsuka, M., Ogo, N., Asai, A., and Akiyama, Y. (2011) Antitumor activity of a novel small molecule STAT3 inhibitor against a human lymphoma cell line with high STAT3 activation. *Int. J. Oncol.* 38, 1245–1252.
- Astronomo, R. D., and Burton, D. R. (2010) Carbohydrate vaccines : developing sweet solutions to sticky situations ? *Nat. Rev. Drug Discov.* 9, 308–324.
- Bay, S., Lo-Man, R., Osinaga, E., Nakada, H., Leclerc, C., and Cantacuzene, D. (1997) Preparation of a multiple antigen glycopeptide (MAG) carrying the Tn antigen. A possible approach to a synthetic carbohydrate vaccine. *J. Pept. Res.* 49, 620–625.
- Bendelac, A., Savage, P. B., and Teyton, L. (2007) The Biology of NKT Cells. *Annu. Rev. Immunol.* 25, 297–336.
- Berti, F., and Adamo, R. (2013) Recent Mechanistic Insights on Glycoconjugate Vaccines and Future Perspectives. *ACS Chem. Biol.* 8, 1653–1663.
- Bettahi, I., Dasgupta, G., Renaudet, O., Chentoufi, A. A., Zhang, X., Carpenter, D., Yoon, S., Dumy, P., and BenMohamed, L. (2009) Antitumor activity of a self-adjuvanting glyco-lipopeptide vaccine bearing B cell, CD4+ and CD8+ T cell epitopes. *Cancer Immunol. Immunother.* 58, 187–200.
- Bilodeau, M. T., Park, T. K., Hu, S., Randolph, J. T., Danishefsky, S. J., Livingston, P. O., and Zhang, S. (1995) Total Synthesis of a Human Breast Tumor Associated Antigen. *J. Am. Chem. Soc.* 117, 7840–7841.
- Biswas, K., Coltart, D. M., and Danishefsky, S. J. (2002) Construction of carbohydrate-based antitumor vaccines : synthesis of glycosyl amino acids by olefin cross-metathesis. *Tetrahedron Lett.* 43, 6107–6110.
- Boes, M. (2000) Role of natural and immune IgM antibodies in immune responses. *Mol. Immunol.* 37, 1141–1149.
- Boland, C. R., and Ricciardiello, L. (1999) How many mutations does it take to make a tumor ? *Proc. Natl. Acad. Sci. U. S. A.* 96, 14675–14677.
- Bondalapati, S., Jbara, M., and Brik, A. (2016) Expanding the chemical toolbox for the synthesis of large and uniquely modified proteins. *Nat Chem* 8, 407–418.

- Bonnat, L., Bar, L., Génaro, B., Bonnet, H., Jarjayes, O., Thomas, F., Dejeu, J., Defrancq, E., and Lavergne, T. (2017) Template-Mediated Stabilization of a DNA G-Quadruplex formed in the HIV-1 Promoter and Comparative Binding Studies. *Chem. – A Eur. J.* 23, 5602–5613.
- Borges, E., Wiesmüller, K.-H., Jung, G., and Walden, P. (1994) Efficacy of synthetic vaccines in the induction of cytotoxic T lymphocytes comparison of the costimulating support provided by helper T cells and lipoamino acid. *J. Immunol. Methods* 173, 253–263.
- Buskas, T., Ingale, S., and Boons, G.-J. (2005) Towards a Fully Synthetic Carbohydrate-Based Anticancer Vaccine : Synthesis and Immunological Evaluation of a Lipidated Glycopeptide Containing the Tumor-Associated Tn Antigen. *Angew. Chemie Int. Ed.* 44, 5985–5988.
- Buskas, T., Li, Y., and Boons, G.-J. (2004) The Immunogenicity of the Tumor-Associated Antigen Lewisy May Be Suppressed by a Bifunctional Cross-Linker Required for Coupling to a Carrier Protein. *Chem. – A Eur. J.* 10, 3517–3524.
- Cato, D., Buskas, T., and Boons, G. (2005) Highly Efficient Stereospecific Preparation of Tn and TF Building Blocks Using Thioglycosyl Donors and the Ph<sub>2</sub>SO/Tf<sub>2</sub>O Promotor System. *J. Carbohydr. Chem.* 24, 503–516.
- Cecioni, S., Imberty, A., and Vidal, S. (2015) Glycomimetics versus Multivalent Glycoconjugates for the Design of High Affinity Lectin Ligands. *Chem. Rev.* 115, 525–561.
- Chomez, P., De Backer, O., Bertrand, M., De Plaen, E., Boon, T., and Lucas, S. (2001) An Overview of the MAGE Gene Family with the Identification of All Human Members of the Family. *Cancer Res.* 61, 5544–5551.
- Chu, R. S., Targoni, O. S., Krieg, A. M., Lehmann, P. V, and Harding, C. V. (1997) CpG Oligodeoxynucleotides Act as Adjuvants that Switch on T Helper 1 (Th1) Immunity . *J. Exp. Med.* 186, 1623–1631.
- Cipolla, L., Rescigno, M., Leone, A., Peri, F., La Ferla, B., and Nicotra, F. (2002) Novel Tn antigen-containing neoglycopeptides : synthesis and evaluation as anti tumor vaccines. *Bioorg. Med. Chem.* 10, 1639–1646.
- Cohn, M., Av Mitchison, N., Paul, W. E., Silverstein, A. M., Talmage, D. W., and Weigert, M. (2007) Reflections on the clonal-selection theory. *Nat Rev Immunol* 7, 823–830.
- Coley, W. B. (1893) The treatment of malignant tumours by repeated inoculations of erysipelas : with a report of ten original cases. *Am. J. Med. Sci.* 105, 487–511.
- Corzana, F., Busto, J. H., García de Luis, M., Jiménez-Barbero, J., Avenoza, A., and Peregrina, J. M. (2009) The Nature and Sequence of the Amino Acid Aglycone Strongly Modulates the Conformation and Dynamics Effects of Tn Antigen's Clusters. *Chem. – A Eur. J.* 15, 3863–3874.
- Couzin-Frankel, J. (2013) Cancer Immunotherapy. *Science* (80-. ). 342, 1432–1433.
- Dagan, R., Poolman, J., and Siegrist, C. A. (2010) Glycoconjugate vaccines and immune interference : A review. *Vaccine* 28, 5513–5523.
- Danishefsky, S. J., and Bilodeau, M. T. (1996) Glycals in Organic Synthesis : The Evolution of Comprehensive Strategies for the Assembly of Oligosaccharides and Glycoconjugates of Biological Consequence. *Angew. Chemie Int. Ed. English* 35, 1380–1419.
- Danishefsky, S. J., Behar, V., Randolph, J. T., and Lloyd, K. O. (1995) Application of the Glycal Assembly Method to the Concise Synthesis of Neoglycoconjugates of Ley and Leb Blood Group Determinants and of H-Type I and H-Type II Oligosaccharides. *J. Am. Chem. Soc.* 117, 5701–5711.
- de Jong, E. C., Smits, H. H., and Kapsenberg, M. L. (2005) Dendritic cell-mediated T cell polarization. *Springer Semin. Immunopathol.* 26, 289–307.
- Devaud, C., John, L. B., Westwood, J. A., Darcy, P. K., and Kershaw, M. H. (2013) Immune modulation of the tumor microenvironment for enhancing cancer immunotherapy.

Oncoimmunology 2, e25961.

- Disis, M. L., Gooley, T. A., Rinn, K., Davis, D., Piepkorn, M., Cheever, M. A., Knutson, K. L., and Schiffman, K. (2002) Generation of T-Cell Immunity to the HER-2/neu Protein After Active Immunization With HER-2/neu Peptide-Based Vaccines. *J. Clin. Oncol.* 20, 2624–2632.
- Doria-Rose, N. A., and Joyce, M. G. (2015) Strategies to guide the antibody affinity maturation process. *Curr. Opin. Virol.* 11, 137–147.
- Dudley, M. E., Wunderlich, J. R., Robbins, P. F., Yang, J. C., Hwu, P., Schwartzentruber, D. J., Topalian, S. L., Sherry, R., Restifo, N. P., Hubicki, A. M., Robinson, M. R., Raffeld, M., Duray, P., Seipp, C. A., Rogers-Freezer, L., Morton, K. E., Mavroukakis, S. A., White, D. E., and Rosenberg, S. A. (2002) Cancer Regression and Autoimmunity in Patients After Clonal Repopulation with Antitumor Lymphocytes. *Science* (80-. ). 298, 850–854.
- Duthie, M. S., Windish, H. P., Fox, C. B., and Reed, S. G. (2011) Use of defined TLR ligands as adjuvants within human vaccines. *Immunol. Rev.* 239, 178–196.
- Dziadek, S., Kowalczyk, D., and Kunz, H. (2005) Synthetic Vaccines Consisting of Tumor-Associated MUC1 Glycopeptide Antigens and Bovine Serum Albumin. *Angew. Chemie Int. Ed.* 44, 7624–7630.
- El-Mahdi, O., and Melnyk, O. (2013)  $\alpha$ -Oxo Aldehyde or Glyoxylyl Group Chemistry in Peptide Bioconjugation. *Bioconjug. Chem.* 24, 735–765.
- Ercolini, A. M., Machiels, J.-P. H., Chen, Y. C., Slansky, J. E., Giedlen, M., Reilly, R. T., and Jaffee, E. M. (2003) Identification and Characterization of the Immunodominant Rat HER-2/neu MHC Class I Epitope Presented by Spontaneous Mammary Tumors from HER-2/neu-Transgenic Mice. *J. Immunol.* 170, 4273–4280.
- Fallarini, S., Paoletti, T., Battaglini, C. O., Ronchi, P., Lay, L., Bonomi, R., Jha, S., Mancin, F., Scrimin, P., and Lombardi, G. (2013) Factors affecting T cell responses induced by fully synthetic glyco-gold-nanoparticles. *Nanoscale* 5, 390–400.
- Feng, D., Shaikh, A. S., and Wang, F. (2016) Recent Advance in Tumor-associated Carbohydrate Antigens (TACAs)-based Antitumor Vaccines. *ACS Chem. Biol.* 11, 850–863.
- Ferguson, K. M. (2008) Structure-Based View of Epidermal Growth Factor Receptor Regulation. *Annu. Rev. Biophys.* 37, 353–373.
- Fernández-Tejada, A., Brailsford, J., Zhang, Q., Shieh, J.-H., Moore, M. A. S., and Danishefsky, S. J. (2015) Total Synthesis of Glycosylated Proteins – Protein Ligation and Total Synthesis I (Liu, L., Ed.), pp 1–26. Springer International Publishing, Cham.
- Finn, O. J. (2014) Vaccines for Cancer Prevention : A Practical and Feasible Approach to the Cancer Epidemic. *Cancer Immunol. Res.* 2, 708–713.
- Floros, T., and Tarhini, A. A. (2015) Anticancer Cytokines : Biology and Clinical Effects of Interferon- $\gamma$ , Interleukin (IL)-2, IL-15, IL-21, and IL-12. *Semin. Oncol.* 42, 539–548.
- Foged, C., Brodin, B., Frokjaer, S., and Sundblad, A. (2005) Particle size and surface charge affect particle uptake by human dendritic cells in an in vitro model. *Int. J. Pharm.* 298, 315–322.
- Forget, D., Boturyn, D., Defrancq, E., Lhomme, J., and Dumy, P. (2001) Highly efficient synthesis of peptide-oligonucleotide conjugates : Chemoselective oxime and thiazolidine formation. *Chem. – A Eur. J.* 7, 3976–3984.
- Freeman, S. A., Jaumouillé, V., Choi, K., Hsu, B. E., Wong, H. S., Abraham, L., Graves, M. L., Coombs, D., Roskelley, C. D., Das, R., Grinstein, S., and Gold, M. R. (2015) Toll-like receptor ligands sensitize B-cell receptor signalling by reducing actin-dependent spatial confinement of the receptor. *Nat. Commun.* 6, 6168.
- Freund, J. (1947) Some Aspects of Active Immunization. *Annu. Rev. Microbiol.* 1, 291–308.
- Gabius, H. J., and Roth, J. (2017) An introduction to the sugar code. *Histochem. Cell Biol.* 147,

111–117.

- Gamblin, D. P., Scanlan, E. M., and Davis, B. G. (2009) Glycoprotein Synthesis : An Update. *Chem. Rev.* 109, 131–163.
- Genbacev, O. D., Prakobphol, A., Foulk, R. A., Krtolica, A. R., Ilic, D., Singer, M. S., Yang, Z.-Q., Kiessling, L. L., Rosen, S. D., and Fisher, S. J. (2003) Trophoblast L-Selectin-Mediated Adhesion at the Maternal-Fetal Interface. *Science* (80- ). 299, 405–408.
- Gildersleeve, J. C., Oyelaran, O., Simpson, J. T., and Allred, B. (2008) Improved Procedure for Direct Coupling of Carbohydrates to Proteins via Reductive Amination. *Bioconjug. Chem.* 19, 1485–1490.
- Gildersleeve, J. C., Wang, B., Achilefu, S., Tu, Z., and Xu, M. (2012) Glycan array analysis of the antigen repertoire targeted by tumor-binding antibodies. *Bioorg. Med. Chem. Lett.* 22, 6839–6843.
- Gilewski, T., Ragupathi, G., Bhuta, S., Williams, L. J., Musselli, C., Zhang, X.-F., Bencsath, K. P., Panageas, K. S., Chin, J., Hudis, C. A., Norton, L., Houghton, A. N., Livingston, P. O., and Danishefsky, S. J. (2001) Immunization of metastatic breast cancer patients with a fully synthetic globo H conjugate : A phase I trial. *Proc. Natl. Acad. Sci.* 98, 3270–3275.
- Góngora-Benítez, M., Tulla-Puche, J., and Albericio, F. (2014) Multifaceted Roles of Disulfide Bonds. *Peptides as Therapeutics. Chem. Rev.* 114, 901–926.
- Grigalevicius, S., Chierici, S., Renaudet, O., Lo-Man, R., Dériaud, E., Leclerc, C., and Dumy, P. (2005) Chemoselective assembly and immunological evaluation of multiepitopic glycoconjugates bearing clustered Tn antigen as synthetic anticancer vaccines. *Bioconjug. Chem.* 16, 1149–1159.
- Groscurth, P., and Filgueira, L. (1998) Killing Mechanisms of Cytotoxic T Lymphocytes. *Physiology* 13, 17–21.
- Gulley, J. L., Madan, R. A., and Schlom, J. (2011) Impact of tumour volume on the potential efficacy of therapeutic vaccines. *Curr. Oncol.* 18, 150–157.
- Guo, C., Manjili, M. H., Subjeck, J. R., Sarkar, D., Fisher, P. B., and Wang, X. Y. (2013) Therapeutic cancer vaccines. Past, present, and future. *Adv. Cancer Res.* 119, 421–475.
- Hällbrink, M., Florén, A., Elmquist, A., Pooga, M., Bartfai, T., and Langel, Ü. (2001) Cargo delivery kinetics of cell-penetrating peptides. *Biochim. Biophys. Acta – Biomembr.* 1515, 101–109.
- Hamley, I. W. (2015) Lipopeptides : from self-assembly to bioactivity. *Chem. Commun.* 51, 8574–8583.
- Hamley, I. W., Kirkham, S., Dehsorkhi, A., Castelletto, V., Reza, M., and Ruokolainen, J. (2014) Toll-like receptor agonist lipopeptides self-assemble into distinct nanostructures. *Chem. Commun.* 50, 15948–15951.
- Hanisch, F.-G., and Müller, S. (2000) MUC1 : the polymorphic appearance of a human mucin. *Glycobiology* 10, 439–449.
- Hardwick, N., and Chain, B. (2011) Epitope spreading contributes to effective immunotherapy in metastatic melanoma patients. *Immunotherapy* 3, 731–733.
- Hein, W. R., and Griebel, P. J. (2003) A road less travelled : large animal models in immunological research. *Nat Rev Immunol* 3, 79–84.
- Helling, F., Shang, A., Calves, M., Zhang, S., Ren, S., Yu, R. K., Oettgen, H. F., and Livingston, P. O. (1994) GD3 Vaccines for Melanoma : Superior Immunogenicity of Keyhole Limpet Hemocyanin Conjugate Vaccines. *Cancer Res.* 54, 197–203.
- Herzenberg, L. A., Tokuhiya, T., and Herzenberg, L. A. (1980) Carrier-priming leads to hapten-specific suppression. *Nature* 285, 664–667.
- Huang, S., Rutkowsky, J. M., Snodgrass, R. G., Ono-Moore, K. D., Schneider, D. A., Newman, J. W., Adams, S. H., and Hwang, D. H. (2012) Saturated fatty acids activate TLR-mediated proinflammatory signaling pathways. *J. Lipid Res.* 53, 2002–2013.

- Huang, X., Huang, L., Wang, H., and Ye, X.-S. (2004) Iterative One-Pot Synthesis of Oligosaccharides. *Angew. Chemie Int. Ed.* 43, 5221–5224.
- Ian Storer, R., Aciro, C., and Jones, L. H. (2011) Squaramides : physical properties, synthesis and applications. *Chem. Soc. Rev.* 40, 2330–2346.
- Ingale, S., Buskas, T., and Boons, G.-J. (2006) Synthesis of Glyco(lipo)peptides by Liposome-Mediated Native Chemical Ligation. *Org. Lett.* 8, 5785–5788.
- Ingale, S., Wolfert, M. A., Gaekwad, J., Buskas, T., and Boons, G.-J. (2007) Robust immune responses elicited by a fully synthetic three-component vaccine. *Nat Chem Biol* 3, 663–667.
- Inman, F. P. (1972) *Contemporary Topics in Immunochemistry*. Springer.
- Iwasaki, A., and Medzhitov, R. (2010) Regulation of Adaptive Immunity by the Innate Immune System. *Science* (80-. ). 327, 291 LP-295.
- Jackson, D. C., Lau, Y. F., Le, T., Suhrbier, A., Deliyannis, G., Cheers, C., Smith, C., Zeng, W., and Brown, L. E. (2004) A totally synthetic vaccine of generic structure that targets Toll-like receptor 2 on dendritic cells and promotes antibody or cytotoxic T cell responses. *Proc. Natl. Acad. Sci. United States Am.* 101, 15440–15445.
- Jaffee, E. M., Hruban, R. H., Biedrzycki, B., Laheru, D., Schepers, K., Sauter, P. R., Goemann, M., Coleman, J., Grochow, L., Donehower, R. C., Lillemoe, K. D., O'Reilly, S., Abrams, R. A., Pardoll, D. M., Cameron, J. L., and Yeo, C. J. (2001) Novel Allogeneic Granulocyte-Macrophage Colony-Stimulating Factor–Secreting Tumor Vaccine for Pancreatic Cancer : A Phase I Trial of Safety and Immune Activation. *J. Clin. Oncol.* 19, 145–156.
- Jegerlehner, A., Storni, T., Lipowsky, G., Schmid, M., Pumpens, P., and Bachmann, M. F. (2002) Regulation of IgG antibody responses by epitope density and CD21-mediated costimulation. *Eur. J. Immunol.* 32, 3305–3314.
- Jiménez-Barbero, J., Dragoni, E., Venturi, C., Nannucci, F., Ardá, A., Fontanella, M., André, S., Cañada, F. J., Gabius, H.-J., and Nativi, C. (2009)  $\alpha$ -O-Linked Glycopeptide Mimetics : Synthesis, Conformation Analysis, and Interactions with Viscumin, a Galactoside-Binding Model Lectin. *Chem. – A Eur. J.* 15, 10423–10431.
- Jung, J. P., Nagaraj, A. K., Fox, E. K., Rudra, J. S., Devgun, J. M., and Collier, J. H. (2009) Co-assembling peptides as defined matrices for endothelial cells. *Biomaterials* 30, 2400–2410.
- Kagan, E., Ragupathi, G., Yi, S. S., Reis, C. A., Gildersleeve, J., Kahne, D., Clausen, H., Danishefsky, S. J., and Livingston, P. O. (2005) Comparison of antigen constructs and carrier molecules for augmenting the immunogenicity of the monosaccharide epithelial cancer antigen Tn. *Cancer Immunol. Immunother.* 54, 424–430.
- Kaiser, A., Gaidzik, N., Westerlind, U., Kowalczyk, D., Hobel, A., Schmitt, E., and Kunz, H. (2009) A synthetic vaccine consisting of a tumor-associated sialyl-T NMUC1 tandem-repeat glycopeptide and tetanus toxoid : induction of a strong and highly selective immune response. *Angew. Chemie – Int. Ed.* 48, 7551–7555.
- Kalka-Moll, W. M., Tzianabos, A. O., Bryant, P. W., Niemeyer, M., Ploegh, H. L., and Kasper, D. L. (2002) Zwitterionic Polysaccharides Stimulate T Cells by MHC Class II-Dependent Interactions. *J. Immunol.* 169, 6149–6153.
- Kaltgrad, E., Sen Gupta, S., Punna, S., Huang, C.-Y., Chang, A., Wong, C.-H., Finn, M. G., and Blixt, O. (2007) Anti-Carbohydrate Antibodies Elicited by Polyvalent Display on a Viral Scaffold. *ChemBioChem* 8, 1455–1462.
- Kantoff, W. P., Higano, S. C., Shore, D. N., Berger, R. E., Small, J. E., Penson, F. D., Redfern, H. C., Ferrari, C. A., Dreicer, R., Sims, B. R., Xu, Y., Frohlich, W. M., and Schellhammer, F. P. (2010) Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. *N. Engl. J. Med.* 363, 411–422.

- Kawashima, I., Kotani, M., Ozawa, H., Suzuki, M., and Tai, T. (1994) Generation of monoclonal antibodies specific for ganglioside lactones : Evidence of the expression of lactone on human melanoma cells. *Int. J. Cancer* 58, 263–268.
- Keil, S., Claus, C., Dippold, W., and Kunz, H. (2001) Towards the development of antitumor vaccines : A synthetic conjugate of a tumor-associated MUC1 glycopeptide antigen and a tetanus toxin epitope. *Angew. Chemie – Int. Ed.* 40, 366–369.
- Kennedy, R., and Celis, E. (2008) Multiple roles for CD4 + T cells in anti-tumor immune responses. *Immunol. Rev.* 222, 129–144.
- Kiessling, L. L., and Grim, J. C. (2013) Glycopolymer probes of signal transduction. *Chem. Soc. Rev.* 42, 4476–4491.
- Kirkwood, J. M., Butterfield, L. H., Tarhini, A. A., Zarour, H., Kalinski, P., and Ferrone, S. (2012) Immunotherapy of cancer in 2012. *CA. Cancer J. Clin.* 62, 309–335.
- Kufe, D. W. (2009) Mucins in cancer : function, prognosis and therapy. *Nat Rev Cancer* 9, 874–885.
- Kunz, H., and Birnbach, S. (1986) Synthesis of O-Glycopeptides of the Tumor-Associated TN- and T-Antigen Type and Their Binding to Bovine Serum Albumin. *Angew. Chemie Int. Ed. English* 25, 360–362.
- Kurosaka, A., Kitagawa, H., Fukui, S., Numata, Y., Nakada, H., Funakoshi, I., Kawasaki, T., Ogawa, T., Iijima, H., and Yamashina, I. (1988) A monoclonal antibody that recognizes a cluster of a disaccharide, NeuAc $\alpha$ 2 $\beta$ GalNAc, in mucin-type glycoproteins. *J. Biol. Chem.* 263, 8724–8726.
- Kurosaki, T., Kometani, K., and Ise, W. (2015) Memory B cells. *Nat. Rev. Immunol.* 15, 149–159.
- Kurts, C., Robinson, B. W. S., and Knolle, P. A. (2010) Cross-priming in health and disease. *Nat. Publ. Gr.* 10, 403–414.
- Kwon, D. S., Gregorio, G., Bitton, N., Hendrickson, W. A., and Littman, D. R. (2002) DC-SIGN-Mediated Internalization of HIV Is Required for Trans-Enhancement of T Cell Infection. *Immunity* 16, 135–144.
- Lau, S. K., Weiss, L. M., and Chu, P. G. (2004) Differential Expression of MUC1, MUC2, and MUC5AC in Carcinomas of Various Sites An Immunohistochemical Study. *Am. J. Clin. Pathol.* 122, 61–69.
- Laubreton, D., Bay, S., Sedlik, C., Artaud, C., Ganneau, C., Dériaud, E., Viel, S., Puaux, A.-L., Amigorena, S., Gérard, C., Lo-Man, R., and Leclerc, C. (2016) The fully synthetic MAG-Tn3 therapeutic vaccine containing the tetanus toxoid-derived TT830-844 universal epitope provides anti-tumor immunity. *Cancer Immunol. Immunother.* 65, 315–325.
- Leclerc, C., Dériaud, E., Mimic, V., and van der Werf, S. (1991) Identification of a T-cell epitope adjacent to neutralization antigenic site 1 of poliovirus type 1. *J. Virol.* 65, 711–718.
- Lee, H.-C., Butler, M., and Wu, S.-C. (2012) Using recombinant DNA technology for the development of live-attenuated dengue vaccines. *Enzyme Microb. Technol.* 51, 67–72.
- Lin, T. (2006) Structural genesis of the chemical addressability in a viral nano-block. *J. Mater. Chem.* 16, 3673–3681.
- Livingston, P. O. (1995) Approaches to Augmenting the Immunogenicity of Melanoma Gangliosides : From Whole Melanoma Cells to Ganglioside-KLH Conjugate Vaccines. *Immunol. Rev.* 145, 147–166.
- Livingston, P. O., Natoli, E. J., Calves, M. J., Stockert, E., Oettgen, H. F., and Old, L. J. (1987) Vaccines containing purified GM2 ganglioside elicit GM2 antibodies in melanoma patients. *Proc. Natl. Acad. Sci.* 84, 2911–2915.
- Livingston, P. O., Wong, G. Y., Adluri, S., Tao, Y., Padavan, M., Parente, R., Hanlon, C., Calves,

- M. J., Helling, F., and Ritter, G. (1994) Improved survival in stage III melanoma patients with GM2 antibodies : a randomized trial of adjuvant vaccination with GM2 ganglioside. *J. Clin. Oncol.* 12, 1036–1044.
- Lo-Man, R., Bay, S., Vichier-Guerre, S., Dériaud, E., Cantacuzène, D., and Leclerc, C. (1999) A Fully Synthetic Immunogen Carrying a Carcinoma-associated Carbohydrate for Active Specific Immunotherapy1. *Cancer Res.* 59, 1520–1524.
  - Lo-Man, R., Vichier-Guerre, S., Bay, S., Dériaud, E., Cantacuzène, D., and Leclerc, C. (2001) Anti-Tumor Immunity Provided by a Synthetic Multiple Antigenic Glycopeptide Displaying a Tri-Tn Glycotope. *J. Immunol.* 166, 2849–2854.
  - Lo-Man, R., Vichier-Guerre, S., Perraut, R., Dériaud, E., Huteau, V., BenMohamed, L., Diop, O. M., Livingston, P. O., Bay, S., and Leclerc, C. (2004) A Fully Synthetic Therapeutic Vaccine Candidate Targeting Carcinoma-Associated Tn Carbohydrate Antigen Induces Tumor-Specific Antibodies in Nonhuman Primates. *Cancer Res.* 64, 4987–4994.
  - Lundquist, J. J., and Toone, E. J. (2002) The cluster glycoside effect. *Chem. Rev.* 102, 555–578.
  - Madsen, C. B., Pedersen, A. E., and Wandall, H. H. (2013) Glycan-mediated modification of the immune response. *Oncoimmunology* 2, e23659.
  - Mammen, M., Choi, S.-K., and Whitesides, G. M. (1998) Polyvalent interactions in biological systems : implications for design and use of multivalent ligands and inhibitors. *Angew. Chemie, Int. Ed.* 37, 2755–2794.
  - Mata-Haro, V., Cekic, C., Martin, M., Chilton, P. M., Casella, C. R., and Mitchell, T. C. (2007) The Vaccine Adjuvant Monophosphoryl Lipid A as a TRIF-Biased Agonist of TLR4. *Science* (80- ). 316, 1628–1632.
  - Mazmanian, S. K., and Kasper, D. L. (2006) The love-hate relationship between bacterial polysaccharides and the host immune system. *Nat Rev Immunol* 6, 849–858.
  - McKinney, R. W., and Davenport, F. M. (1961) Studies on the Mechanism of Action of Emulsified Vaccines. *J. Immunol.* 86, 91 LP-100.
  - Melero, I., Gaudernack, G., Gerritsen, W., Huber, C., Parmiani, G., Scholl, S., Thatcher, N., Wagstaff, J., Zielinski, C., Faulkner, I., and Mellstedt, H. (2014) Therapeutic vaccines for cancer : an overview of clinical trials. *Nat. Rev. Clin. Oncol.* 11, 509–524.
  - Metzger, J. W., Wiesmüller, K.-H., and Jung, G. (1991) Synthesis of N<sup>ε</sup>-Fmoc protected derivatives of S-(2,3-dihydroxypropyl)-cysteine and their application in peptide synthesis. *Int. J. Pept. Protein Res.* 38, 545–554.
  - Miermont, A., Barnhill, H., Strable, E., Lu, X., Wall, K. A., Wang, Q., Finn, M. G., and Huang, X. (2008) Cowpea Mosaic Virus Capsid : A Promising Carrier for the Development of Carbohydrate Based Antitumor Vaccines. *Chem. – A Eur. J.* 14, 4939–4947.
  - Miles, D., Roché, H., Martin, M., Perren, T. J., Cameron, D. A., Glaspy, J., Dodwell, D., Parker, J., Mayordomo, J., Tres, A., Murray, J. L., Ibrahim, N. K., and Group, the T. S. (2011) Phase III Multicenter Clinical Trial of the Sialyl-TN (STn)-Keyhole Limpet Hemocyanin (KLH) Vaccine for Metastatic Breast Cancer. *Oncol.* 16, 1092–1100.
  - Mond, J. J., Lees, A., and Snapper, C. M. (1995) T Cell-Independent Antigens Type 2. *Annu. Rev. Immunol.* 13, 655–692.
  - Monsan, P., Remaud-Siméon, M., and André, I. (2010) Transglucosidases as efficient tools for oligosaccharide and glucoconjugate synthesis. *Curr. Opin. Microbiol.* 13, 293–300.
  - Morgan, R. A., Chinnasamy, N., Abate-Daga, D. D., Gros, A., Robbins, P. F., Zheng, Z., Feldman, S. A., Yang, J. C., Sherry, R. M., Phan, G. Q., Hughes, M. S., Kammula, U. S., Miller, A. D., Hessman, C. J., Stewart, A. A., Restifo, N. P., Quezado, M. M., Alimchandani, M., Rosenberg, A. Z., Nath, A., Wang, T., Bielekova, B., Wuest, S. C., Nirmala, A., McMahon, F. J.,

- Wilde, S., Mosetter, B., Schendel, D. J., Laurencot, C. M., and Rosenberg, S. A. (2013) Cancer regression and neurologic toxicity following anti-MAGE-A3 TCR gene therapy. *J. Immunother.* 36, 133–151.
- Mu, C., Despras, G., Lindhorst, T. K., Mu, C., and Mu, C. (2016) Organizing multivalency in carbohydrate recognition. *Chem. Soc. Rev.* 45, 3275–3302.
  - Mutter, M., Hersperger, R., Gubernator, K., and Müller, K. (1989) The construction of new proteins : V. A template-assembled synthetic protein (TASP) containing both a 4-helix bundle and  $\beta$ -barrel-like structure. *Proteins Struct. Funct. Genet.* 5, 13–21.
  - Nakada, H., Inoue, M., Numata, Y., Tanaka, N., Funakoshi, I., Fukui, S., Mellors, A., and Yamashina, I. (1993) Epitopic structure of Tn glycoporphin A for an anti-Tn antibody (MLS 128). *Proc. Natl. Acad. Sci. U. S. A.* 90, 2495–2499.
  - Nakada, H., Inoue, M., Tanaka, N., Numata, Y., Kitagawa, H., Fukui, S., and Yamashina, I. (1991) Expression of the Tn antigen on T-lymphoid cell line Jurkat. *Biochem. Biophys. Res. Commun.* 179, 762–767.
  - Nakamori, S., Ota, D. M., Cleary, K. R., Shirotani, K., and Irimura, T. (1994) MUC1 mucin expression as a marker of progression and metastasis of human colorectal carcinoma. *Gastroenterology* 106, 353–361.
  - Nath, S., and Mukherjee, P. (2017) MUC1 : a multifaceted oncoprotein with a key role in cancer progression. *Trends Mol. Med.* 20, 332–342.
  - Nimmerjahn, F., and Ravetch, J. V. (2008) Fc $\gamma$  receptors as regulators of immune responses. *Nat Rev Immunol* 8, 34–47.
  - Nishat, S., and Andreatina, R. P. (2016) Entirely Carbohydrate-Based Vaccines : An Emerging Field for Specific and Selective Immune Responses. *Vaccines* .
  - Numata, Y., Nakada, H., Fukui, S., Kitagawa, H., Ozaki, K., Inoue, M., Kawasaki, T., Funakoshi, I., and Yamashina, I. (1990) A monoclonal antibody directed to Tn antigen. *Biochem. Biophys. Res. Commun.* 170, 981–985.
  - O'Neill, L. A. J., Golenbock, D., and Bowie, A. G. (2013) The history of Toll-like receptors – redefining innate immunity. *Nat Rev Immunol* 13, 453–460.
  - Ott, G., and Van Nest, G. (2007) Development of Vaccine Adjuvants : A Historical Perspective, in *Vaccine Adjuvants and Delivery Systems*, pp 1–31. John Wiley & Sons, Inc.
  - Oyelaran, O., and Gildersleeve, J. C. (2010) Evaluation of human antibody responses to keyhole limpet hemocyanin on a carbohydrate microarray. *Proteomics – Clin. Appl.* 4, 285–294.
  - Parry, A. L., Clemson, N. A., Ellis, J., Bernhard, S. S. R., Davis, B. G., and Cameron, N. R. (2013) “Multicopy Multivalent” Glycopolymer-Stabilized Gold Nanoparticles as Potential Synthetic Cancer Vaccines. *J. Am. Chem. Soc.* 135, 9362–9365.
  - Parslow, A., Parakh, S., Lee, F.-T., Gan, H., and Scott, A. (2016) Antibody–Drug Conjugates for Cancer Therapy. *Biomedicines* 4, 14.
  - Partis, M. D., Griffiths, D. G., Roberts, G. C., and Beechey, R. B. (1983) Cross-linking of protein by  $\beta$ -maleimido alkanoylN-hydroxysuccinimido esters. *J. Protein Chem.* 2, 263–277.
  - Peri, F. (2013) Clustered carbohydrates in synthetic vaccines. *Chem. Soc. Rev.* 42, 4543–4556.
  - Pifferi, C., Berthet, N., and Renaudet, O. (2017) Cyclopeptide scaffolds in carbohydrate-based synthetic vaccines. *Biomater. Sci.* 5, 953–965.
  - Pifferi, C., Daskhan, G. C., Fiore, M., Shiao, T. C., Roy, R., and Renaudet, O. (2017) Aminoxyated Carbohydrates : Synthesis and Applications. *Chem. Rev.* 117, 9839–9873.
  - Pomés, A., Chruszcz, M., Gustchina, A., Minor, W., Mueller, G. A., Pedersen, L. C., Wlodawer, A., and Chapman, M. D. (2017) 100 Years later : Celebrating the contributions of x-ray crystallography to allergy and clinical immunology. *J. Allergy Clin. Immunol.* 136, 29–37.e10.



- Posnett, D. N., Mcgrath, H., and Tam, P. (1988) A Novel Method for Producing Anti-peptide Antibodies. *Biochemistry* 263, 1719–1725.
- Puffer, E. B., Pontrello, J. K., Hollenbeck, J. J., Kink, J. A., and Kiessling, L. L. (2007) Activating B Cell Signaling with Defined Multivalent Ligands. *ACS Chem. Biol.* 2, 252–262.
- Ragupathi, G., Cappello, S., Yi, S. S., Canter, D., Spassova, M., Bornmann, W. G., Danishefsky, S. J., and Livingston, P. O. (2002) Comparison of antibody titers after immunization with monovalent or tetravalent KLH conjugate vaccines. *Vaccine* 20, 1030–1038.
- Ragupathi, G., Coltart, D. M., Williams, L. J., Koide, F., Kagan, E., Allen, J., Harris, C., Glunz, P. W., Livingston, P. O., and Danishefsky, S. J. (2002) On the power of chemical synthesis : Immunological evaluation of models for multiantigenic carbohydrate-based cancer vaccines. *Proc. Natl. Acad. Sci.* 99, 13699–13704.
- Ragupathi, G., Koide, F., Livingston, P. O., Cho, Y. S., Endo, A., Wan, Q., Spassova, M. K., Keding, S. J., Allen, J., Ouerfelli, O., Wilson, R. M., and Danishefsky, S. J. (2006) Preparation and Evaluation of Unimolecular Pentavalent and Hexavalent Antigenic Constructs Targeting Prostate and Breast Cancer : A Synthetic Route to Anticancer Vaccine Candidates. *J. Am. Chem. Soc.* 128, 2715–2725.
- Ragupathi, G., Koide, F., Sathyan, N., Kagan, E., Spassova, M., Bornmann, W., Gregor, P., Reis, C. A., Clausen, H., Danishefsky, S. J., and Livingston, P. O. (2003) A preclinical study comparing approaches for augmenting the immunogenicity of a heptavalent KLH-conjugate vaccine against epithelial cancers. *Cancer Immunol. Immunother.* 52, 608–616.
- Ragupathi, G., Meyers, M., Adluri, S., Howard, L., Musselli, C., and Livingston, P. O. (2000) Induction of antibodies against GD3 ganglioside in melanoma patients by vaccination with GD3-lactone-KLH conjugate plus immunological adjuvant QS-21. *Int. J. Cancer* 85, 659–666.
- Ragupathi, G., Rao Koganty, R., Qiu, D., Lloyd, K. O., and Livingston, P. O. (1998) A novel and efficient method for synthetic carbohydrate conjugate vaccine preparation : synthesis of sialyl Tn-KLH conjugate using a 4-(4-N-maleimidomethyl) cyclohexane-1-carboxyl hydrazide (MMCCH) linker arm. *Glycoconj. J.* 15, 217–221.
- Renaudet, O., BenMohamed, L., Dasgupta, G., Bettahi, I., and Dumy, P. (2008) Towards a self-adjuvanting multivalent B and T cell epitope containing synthetic glycolipopeptide cancer vaccine. *ChemMedChem* 3, 737–741.
- Renaudet, O., Dasgupta, G., Bettahi, I., Shi, A., Nesburn, A. B., Dumy, P., and BenMohamed, L. (2010) Linear and branched glyco-lipopeptide vaccines follow distinct cross-presentation pathways and generate different magnitudes of antitumor immunity. *PLoS One* 5.
- Richichi, B., Thomas, B., Fiore, M., Bosco, R., Qureshi, H., Nativi, C., Renaudet, O., and BenMohamed, L. (2014) A Cancer Therapeutic Vaccine based on Clustered Tn-Antigen Mimetics Induces Strong Antibody-Mediated Protective Immunity. *Angew. Chemie Int. Ed.* 53, 11917–11920.
- Rickert, R. C. (2005) Regulation of B lymphocyte activation by complement C3 and the B cell coreceptor complex. *Curr. Opin. Immunol.* 17, 237–243.
- Roldão, A., Mellado, M. C. M., Castilho, L. R., Carrondo, M. J. T., and Alves, P. M. (2010) Virus-like particles in vaccine development. *Expert Rev. Vaccines* 9, 1149–1176.
- Rosenberg, S. A., and Restifo, N. P. (2015) Adoptive cell transfer as personalized immunotherapy for human cancer. *Science* (80-. ). 348, 62–68.
- Röttschke, O., Falk, K., Stevanovic, S., Jung, G., Walden, P., and Rammensee, H.-G. (1991) Exact prediction of a natural T cell epitope. *Eur. J. Immunol.* 21, 2891–2894.
- Rudra, J. S., Tian, Y. F., Jung, J. P., and Collier, J. H. (2010) A self-assembling peptide acting as an immune adjuvant. *Proc. Natl. Acad. Sci.* 107, 622–627.

- Saeland, E., van Vliet, S. J., Bäckström, M., van den Berg, V. C. M., Geijtenbeek, T. B. H., Meijer, G. A., and van Kooyk, Y. (2007) The C-type lectin MGL expressed by dendritic cells detects glycan changes on MUC1 in colon carcinoma. *Cancer Immunol. Immunother.* 56, 1225–1236.
- Scher, H. I., Eisenberger, M., D'Amico, A. V., Halabi, S., Small, E. J., Morris, M., Kattan, M. W., Roach, M., Kantoff, P., Pienta, K. J., Carducci, M. A., Agus, D., Slovin, S. F., Heller, G., Kelly, W. K., Lange, P. H., Petrylak, D., Berg, W., Higano, C., Wilding, G., Moul, J. W., Partin, A. N., Logothetis, C., and Soule, H. R. (2004) Eligibility and Outcomes Reporting Guidelines for Clinical Trials for Patients in the State of a Rising Prostate-Specific Antigen : Recommendations From the Prostate-Specific Antigen Working Group. *J. Clin. Oncol.* 22, 537–556.
- Seeberger, P. H. (2015) The Logic of Automated Glycan Assembly. *Acc. Chem. Res.* 48, 1450–1463.
- Seya, T., Shime, H., Takeda, Y., Tatematsu, M., Takashima, K., and Matsumoto, M. (2015) Adjuvant for vaccine immunotherapy of cancer – focusing on Toll-like receptor 2 and 3 agonists for safely enhancing antitumor immunity. *Cancer Sci.* 106, 1659–1668.
- Shi, M., Kleski, K. A., Trabbic, K. R., Bourgault, J.-P., and Andreana, P. R. (2016) Sialyl-Tn Polysaccharide A1 as an Entirely Carbohydrate Immunogen : Synthesis and Immunological Evaluation. *J. Am. Chem. Soc.* 138, 14264–14272.
- Slovin, S. F., Keding, S. J., and Ragupathi, G. (2005) Carbohydrate vaccines as immunotherapy for cancer. *Immunol. Cell Biol.* 83, 418–428.
- Slovin, S. F., Ragupathi, G., Musselli, C., Fernandez, C., Diani, M., Verbel, D., Danishefsky, S., Livingston, P., and Scher, H. I. (2005) Thomsen-Friedenreich (TF) antigen as a target for prostate cancer vaccine : clinical trial results with TF cluster (c)-KLH plus QS21 conjugate vaccine in patients with biochemically relapsed prostate cancer. *Cancer Immunol. Immunother.* 54, 694–702.
- Soares, M. M., Mehta, V., and Finn, O. J. (2001) Three Different Vaccines Based on the 140-Amino Acid MUC1 Peptide with Seven Tandemly Repeated Tumor-Specific Epitopes Elicit Distinct Immune Effector Mechanisms in Wild-Type Versus MUC1-Transgenic Mice with Different Potential for Tumor Rejection. *J. Immunol.* 166, 6555–6563.
- Stumbles, P. A., Himbeck, R., Frelinger, J. A., Collins, E. J., Lake, R. A., and Robinson, B. W. S. (2004) Cutting Edge : Tumor-Specific CTL Are Constitutively Cross-Armed in Draining Lymph Nodes and Transiently Disseminate to Mediate Tumor Regression following Systemic CD40 Activation. *J. Immunol.* 173, 5923–5928.
- Svennerholm, L. (1957) Quantitative estimation of sialic acids. *Biochim. Biophys. Acta* 24, 604–611.
- Takeda, K., Kojima, Y., Uno, T., Hayakawa, Y., Teng, M. W. L., Yoshizawa, H., Yagita, H., Gejyo, F., Okumura, K., and Smyth, M. J. (2010) Combination Therapy of Established Tumors by Antibodies Targeting Immune Activating and Suppressing Molecules. *J. Immunol.* 184, 5493–5501.
- Tang, C.-K., and Apostolopoulos, V. (2008) Strategies used for MUC1 immunotherapy : preclinical studies. *Expert Rev. Vaccines* 7, 951–962.
- Tang, W., and Becker, M. L. (2014) “Click” reactions : a versatile toolbox for the synthesis of peptide-conjugates. *Chem. Soc. Rev.* 43, 7013–7039.
- Tangye, S. G., Ferguson, A., Avery, D. T., Ma, C. S., and Hodgkin, P. D. (2002) Isotype Switching by Human B Cells Is Division-Associated and Regulated by Cytokines. *J. Immunol.* 169, 4298–4306.
- Therasse, P., Eisenhauer, E. A., and Verweij, J. (2017) RECIST revisited : A review of validation studies on tumour assessment. *Eur. J. Cancer* 42, 1031–1039.
- Treanor, B. (2012) B-cell receptor : From resting state to activate. *Immunology* 136, 21–27.

- 
- Vinay, D. S., Ryan, E. P., Pawelec, G., Talib, W. H., Stagg, J., Elkord, E., Lichtor, T., Decker, W. K., Whelan, R. L., Kumara, H. M. C. S., Signori, E., Honoki, K., Georgakilas, A. G., Amin, A., Helferich, W. G., Boosani, C. S., Guha, G., Ciriolo, M. R., Chen, S., Mohammed, S. I., Azmi, A. S., Keith, W. N., Bilsland, A., Bhakta, D., Halicka, D., Fujii, H., Aquilano, K., Ashraf, S. S., Nowsheen, S., Yang, X., Choi, B. K., and Kwon, B. S. (2015) Immune evasion in cancer : Mechanistic basis and therapeutic strategies. *Semin. Cancer Biol.* 35, S185–S198.
  - Walker, L. S. K. (2017) PD-1 and CTLA-4 : Two checkpoints, one pathway ? *Sci. Immunol.* 2.
  - Wang, Q., Kaltgrad, E., Lin, T., Johnson, J. E., and Finn, M. G. (2002) Natural Supramolecular Building Blocks. *Chem. Biol.* 9, 805–811.
  - Ward, S., Casey, D., Labarthe, M.-C., Whelan, M., Dalgleish, A., Pandha, H., and Todryk, S. (2002) Immunotherapeutic potential of whole tumour cells. *Cancer Immunol. Immunother.* 51, 351–357.
  - White, J. L., and Schlageter, E. A. (1934) Diphtheria toxoid : Comparative immunizing value with and with-out alum, as indicated by the schick test. *J. Am. Med. Assoc.* 102, 915.
  - Wilkinson, B. L., Day, S., Malins, L. R., Apostolopoulos, V., and Payne, R. J. (2011) Self-Adjuvanting Multicomponent Cancer Vaccine Candidates Combining Per-Glycosylated MUC1 Glycopeptides and the Toll-like Receptor 2 Agonist Pam3CysSer. *Angew. Chemie Int. Ed.* 50, 1635–1639.
  - Wong, H. H., Lemoine, N. R., and Wang, Y. (2010) Oncolytic Viruses for Cancer Therapy : Overcoming the Obstacles. *Viruses* 2, 78–106.
  - Zhang, S., Cordon-Cardo, C., Zhang, H. S., Reuter, V. E., Adluri, S., Hamilton, W. B., Lloyd, K. O., and Livingston, P. O. (1997) Selection of tumor antigens as targets for immune attack using immunohistochemistry : I. Focus on gangliosides. *Int J Cancer* 73, 42–49.
  - Zhang, S., Cordon-Cardo, C., Zhang, H. S., Reuter, V. E., Adluri, S., Hamilton, W. B., Lloyd, K. O., and Livingston, P. O. (1997) Selection of tumor antigens as targets for immune attack using immunohistochemistry : II. Blood group-related antigens. *Int J Cancer* 73, 50–56.
  - Zhu, J., Wan, Q., Lee, D., Yang, G., Spassova, M. K., Ouerfelli, O., Ragupathi, G., Damani, P., Livingston, P. O., and Danishefsky, S. J. (2009) From Synthesis to Biologics : Preclinical Data on a Chemistry Derived Anticancer Vaccine. *J. Am. Chem. Soc.* 131, 9298–9303.