Babensee captions (from version modified 5/13/15)

Figure 1. (*a–c*) Overview of interactions of different types and structures of biomaterials with the immune system. Abbreviations: Ig, immunoglobulin; IL-10, interleukin-10; MPLA, monophosphoryl lipid A; PEG, polyethylene glycol; PLGA, poly(lactic-*co*-glycolic) acid; PRR, pattern recognition receptor; TGF-β, transforming growth factor-β; TLR, Toll-like receptor; lymph, lymph node; conj., conjugated.

Figure 2. Nano- or microparticle engineering for immune outcomes. (*a*) Scanning electron microscope and transmission electron microscope (*inset*) images of budding and spherical polystyrene-*b*-poly(ethylene oxide) microparticles. (*b*) Confocal microscopy images of macrophage-associated (*red*) budding and spherical particles, (*green*) lysosomes, (*blue*) nuclei. (*c--d*) Particle-induced neutrophil recruitment (*c*) and interleukin (IL)-1β cytokine secretion (*d*) depends on surface curvature. (*e*) Dendritic cell (DC) inflammatory maturation factor (IMF) levels in response to glycoconjugate adsorbed to wells with different surface properties. The molar ratio of thiolated glycan to bovine serum albumin (BSA) is indicated. The isoelectric point (pI) of glycoconjugates of BSAwas scaled from a pI of ~4.0 to ~10.0 using ethylenediamine (EDA). NC-BSA: no EDA added; L-BSA: 0.05 M EDA, low pI; M-BSA: 0.15 M EDA, medium pI; H-BSA: 0.90 M EDA, high pI. (Panels *a--d* adapted with permission from 41; panel *e* adapted with permission from 52.)

Figure 3. Synthetic mast cell (MC) granules for targeted vaccination. (*a*) Scanning electron microscope micrograph of an activated rat peritoneal MC (natural) and a synthetic particle consisting of heparin and chitosan (synthetic). (*b*) Diagram demonstrating the modeling of synthetic particles after MC granules, where chitosan, made positively charged under acidic conditions, is substituted for MC proteases, enabling inflammatory mediators to be entrapped within a similar matrix structure containing heparin. (*c*) Lymph node (LN) sections after injection of saline, particles containing poly-$_L$-lysine conjugated to the fluorochrome fluorescein isothiocyanate (PLL-FITC) (pFITC, *green*) or soluble PLL-FITC (sFITC, *green*). These LNs were isolated 45 minutes post-injection, sectioned, and stained for B cells (B220, *red*) and LN sinuses (Lyve-1, *blue*). (*d*) Day 21 geometric mean titers for total immunoglobulin (Ig) G after vaccination with haemagglutinin in combination with the designated adjuvants, with a boost at day 14. (*e*) Synthetic particles containing tumor necrosis factor (TNF) (pTNF) or the positive control, alum, increased the survival of mice challenged with influenza significantly over naive mice, antigen-alone controls or soluble TNF (sTNF). (Adapted with permission from 89.)

Figure 4. Hitchhiking on lymphocytes. (*a*) Tumor-specific Pmel-1 T cells conjugated with interleukin-15 superagonist (IL-15Sa) and IL-21-releasing nanoparticles (NPs) robustly proliferate in vivo and eradicate established B16 murine melanomas. Dual, longitudinal, in vivo bioluminescence imaging shows the growth of *Gaussia*

luciferase--expressing B16F10 tumors and click beetle red luciferase--expressing T cells. Flow cytometry plots show the frequencies of $V\beta13^{+}CD8^{+}$ tumor-specific T cells recovered from pooled lymph nodes of representative mice 16 days after T cell transfer. (*b, left*) Schematic view of strategy to modulate T cell responses via nanoparticle conjugation to membrane proteins: Surface-conjugated drug-loaded nanoparticles slowly release their cargo compounds, which locally permeate the plasma membrane and block molecules in the cytosol that dampen T cell activation. (*Right*) 3D reconstruction of confocal microscopy images showing $CD8^{+}$ effector T cells (carboxyfluorescein succinimidyl ester stain shown in *blue*) immediately after conjugation with fluorescent, multilamellar lipid vesicles (*yellow*). (*c*) Schematic of T cell--targeted immunoliposome preparation. IL-2-Fc and anti-Thy1.1 F(ab′)2 were mildly reduced by dithiothreitol (DTT) to expose hinge region free thiols (-SH) for reaction with the liposome maleimide functional headgroups. (*d*) Quantification of percentages of endogenous or transferred T cells labeled by day 0 or day 3 liposome (Lip) injections in the blood. (Panel *a* adapted with permission from 133; panel *b* adapted with permission from 134; panels *c* and *d* adapted with permission from 135.)

Figure 5. Injectable and spontaneously assembling scaffolds consisting of mesoporous silica rods (MSRs) modulate immune cells in vivo and increase vaccine efficacy. (*a*) A schematic representation of in vivo spontaneous assembly of MSRs and recruitment of host cells for maturation. PBS: phosphate-buffered saline. (*b*) Enzyme-linked immunosorbent assay (ELISA) analysis of serum ovalbumin (OVA)-specific immunoglobulin (Ig) G2a titers after immunization with, respectively, soluble components of the vaccine (bolus vaccine), MSRs loaded with OVA, or MSR vaccine. (*c*) Number of $tetramer^{+}$ $CD8^{+}$ T cells in spleen 7 days after vaccination with blank MSR (labeled Blank) or complete MSR vaccine (labeled Vaccine). (*d*) Survival rate after subcutaneous injection of various vaccine formulations 10 days before EG.7-OVA tumor inoculation. (Adapted with permission from 156.)