

targets to the lysosomal compartment, but not required for the initial stage(s) of phagocytosis. Mutation of either of the leucine residues individually or in tandem resulted in 70% (p<0.05 compared to wt FcγRIIA) inhibition of internalized targets to co-localize with lysosomes pre-loaded with fluorescent dextran. Mutation of the threonine alone elicited similar results, thus abolishing 78% (p<0.05 compared to wt FcγRIIA) of co-localization. However, when the L-T-L motif was mutated to A-A-A, lysosomal targeting was abolished as observed with tailless FcγRIIA. Therefore, a novel L-T-L motif in the cytoplasmic domain of FcγRIIA is responsible for mediating phagolysosomal fusion. (See also FIG. 1).

### EXAMPLE 3

FcγRIIA wild-type (IIA), various mutants of the L-T-L motif in the cytoplasmic domain of FcγRIIA (IIA(YLTA), IIA(YATL), IIA(YATA), IIA(YAAA)), or FcγRIIA lacking a cytoplasmic domain (IIA(tailless)) were transfected into chinese hamster ovary (CHO) cells. These cells were pre-loaded with fluorescently labeled dextran by incubating the cells with medium containing TRITC-dextran. The cells were then allowed to phagocytose IgG-coated erythrocytes (EA) for 30 minutes. After 30 minutes the cells were placed on ice to stop phagocytosis and observed for location of the internalized EA and TRITC-dextran. Data presented in FIG. 2 are shown as percent of internalized EA colocalized with TRITC-dextran. As shown, mutation of the L-T-L motif inhibits the colocalization (phagolysosome fusion) of the internal EA with TRITC-dextran.

The data presented in FIG. 3 demonstrate that the L-T-L motif mediates specific targeting of internalized targets to fuse with lysosomes. In time-course experiments, the mutant FcγRIIA containing a mutant L-T-L motif, inhibited phagolysosome formation at early time points compared to wild-type FcγRIIA.

To elucidate the mechanism by which the L-T-L motif inhibits phagolysosome fusion, another marker of lysosome location was studied. Lysosome associated membrane protein (LAMP) is a cytosolic protein that colocalizes with lysosomes and the plasma membrane. It was observed that

the L-T-L mutation inhibits the spilling of fluorescent dextran into phagosomes but does not inhibit the acquisition of lysosome associated proteins thus suggesting that phagolysosome formation may be a more complex process than originally thought (see FIG. 4).

The common γ-chain does not mediate efficient phagolysosome fusion. A chimeric molecule was produced containing the ligand-binding domain of FcγRIII and the γ-chain transmembrane and cytoplasmic domain. Upon insertion of the L-T-L motif into the cytoplasmic domain of the chimeric molecule, a 50% increase in phagolysosome formation was observed (see FIG. 5). These data indicate that insertion of the L-T-L motif into a receptor that is not efficient in mediating phagolysosomal fusion can be used to increase the ability of receptors to kill bacterium

All documents cited above are hereby incorporated in their entirety by reference.

What is claimed is:

1. A method of enhancing the ability of a cell to degrade a particle comprising introducing into said cell a nucleic acid sequence encoding an Fc receptor comprising an L-T-L sequence in a cytoplasmic domain thereof, said introduction being effected under conditions such that said nucleic acid sequence is expressed and said enhancement is thereby effected,

wherein said Fc receptor comprises a FcγRIIA cytoplasmic domain modified to comprise at least 1 additional L-T-L peptide.

2. The method according to claim 1 wherein said cell naturally expresses FcγRIIA.

3. The method according to claim 1 wherein said cell does not naturally express FcγRIIA.

4. The method according to claim 1 wherein said cell is an endothelial cell, a fibroblast, a macrophage or an epithelial cell.

5. The method according to claim 1 wherein said particle is a bacterium.

6. The method according to claim 1 wherein said nucleic acid sequence is introduced into said cell in a liposome, a bacterium or a viral vector.

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