Methods: Human umbilical endothelial cells were cultured to confluence and stimulated in the presence of eNOS activity. Phosphorylation of eNOS was analyzed with a phosphospecific eNOS(Ser1179) antibody by Western blotting.

Results: Stimulation (using short term 12-O-tetradecanoylphorbol-13-acetate (TPA) treatment) or inhibition (by GF 109203X) of protein kinase C and IL-4 to differentiate in immature dendritic cells (MDDC). MDDC stimulated by ox-LDL are able to activate T lymphocyte toward a Th1 response similar to that observed during the acute phases of coronary instability.

We hypothesized that LOX-1 could be involved in ox-LDL induced maturation of MDDC and could drive the activation of immune system toward a Th1 response.

Methods: peripheral blood monocyte were collected from healthy donors and CD14+ cells were cultured in the presence of GM-CSF and IL-4 to differentiate in immature dendritic cells and stimulated at day 5 of differentiation by ox-LDL (80 microg/ml) or lipopolysaccharide (LPS) (1 nmol/ml) in the presence and absence of a blocking monoclonal antibody of LOX-1 (10 microg/ml). Analysis of CD80, HLA-DR, CD86, CD14, CD83 expression was performed by flow-cytometry at day 6 of differentiation of DiI labelled ox-LDL by mature dendritic cells were studied by flow-cytometry after maturation induced by LPS or ox-LDL in the presence or absence of LOX-1 antibody.

Results: Pre-treatment with LOX-1 antibody negatively modulates the differentiation of MDDC induced by ox-LDL but not by LPS. Induction of maturation induced by LPS or ox-LDL reduced the amount (mean fluorescence intensities, MFI) of DiI-labelled ox-LDL captured by dendritic cells. Pre-treatment at day 6 of maturation with LOX-1 antibody have no effect in cells stimulated with LPS, conversely in cells stimulated with ox-LDL, LOX-1 antibody reduced by 75% the binding of DiI labelled ox-LDL.

Conclusions: we identified LOX-1 as one of the major receptor involved in up-take of ox-LDL and maturation of MDDC. Moreover activation of MDDC lead to a reorganization of membrane receptor with a dominant role of LOX-1. Inhibition of dendritic cell activation induced by ox-LDL by the use of LOX-1 antibody could have important role in clinical stabilization of patients presenting with ACS.

Tuesday, March 09, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1123-177 Treatment for Children With Idiopathic Pulmonary Arterial Hypertension: Long-Term Survival and Outcomes
Delphine Yung, Greg Maislin, Alison Widlitz, Erika S. Berman Rosenzweig, Kelly Schmitt, Daniela Brady, Ellen O'Brien, Diane Kerstein, Evelyn M. Horn, Robyn J. Barst, Columbia University College of Physicians and Surgeons, New York, NY

Background: For idiopathic pulmonary arterial hypertension (IPAH) in children, it has been calcium channel blockers (CCB) for acute responders (AR) with vasodilator testing and chronic epoprostenol for nonresponders (NR). We sought to determine factors associated with long-term survival and treatment success, i.e., without death or transplant, and without transition to epoprostenol for patients on CCB.

Methods: A previously identified cohort of 79 patients under age 16 diagnosed with IPAH between 1982 and 1995 at Columbia University was followed through 2002.

Results: For AR, survival rates at 1, 5 and 10 years were 97%, 97%, and 81%, respectively. For NR, survival rates on CCB at 1, 5, and 10 years were 84%, 68%, and 47%. Survival rates on epoprostenol at 1, 5, and 10 years were 94%, 81%, and 61%, respectively. Survival rates on epoprostenol at 1, 5, and 10 years were 89%, 63%, and 45%. With multivariate analysis, baseline variables associated with success on CCB were AR status, NYHA class II, III, or IV, and right atrial pressure. When AR status changed to NR status, success on CCB decreased significantly. Both survival and success on epoprostenol were only associated with age at the start of epoprostenol.

Conclusion: These findings suggest that children with IPAH who are AR should be treated with CCB therapy with transition to epoprostenol if they change to NR status. Epoprostenol therapy should be considered in patients with higher NYHA class, and listing for transplantation should be considered in older patients.