



# Characterization of Erythroid Differentiation Related Factor (EDRF), a GATA-1 Regulated Molecular Chaperone for

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**Type of Session:** Plenary

## Background

Molecular chaperone proteins are believed to exist which coordinate the exquisitely controlled translation and folding of globin proteins into functional hemoglobin molecules. These proteins have never been identified.

In an effort to identify these chaperones, downstream targets of GATA-1, a global regulator of hemoglobin synthesis, were isolated. One of these, erythroid differentiation related factor (EDRF) was thought to be a potential chaperone.

The aim of this study was to characterize this novel protein and determine what role, if any, it plays in the coordination of globin chain production

## Materials and Methods

The EDRF gene was identified in G1E cells, an erythroid line derived from embryonic stem cells, using a subtraction-based screening method.

To identify protein interaction partners of EDRF, yeast two-hybrid interaction studies and direct biochemical interaction screens were used.

## Results

Promoter studies indicate that EDRF is directly induced by GATA-1.

α-globin was identified as an EDRF binding partner by both screening methods used. No interaction with β-globin or hemoglobin was found.

The EDRF/alpha globin interaction is concentration dependent in-vitro.

Beta globin competes with EDRF in binding alpha globin. Beta globin binds more tightly, allowing EDRF to surrender alpha globin for orderly assembly of hemoglobin.

EDRF blocks oxidant-induced precipitation of alpha globin.

Simultaneous co-expression of EDRF and alpha globin in COS cells prevented precipitation of excessive alpha globin chains.

## Author's Conclusions

The newly discovered protein, EDRF, functions as a molecular chaperone of alpha globin preventing globin precipitation and cell apoptosis in red cells during hemoglobin synthesis.

EDRF forms a stable complex with alpha globin.

EDRF blocks alpha globin precipitation in solution and in live cells.

Little is known about regulation of EDRF transcription other than its promoter binding site for GATA-1

### **Clinical/Scientific Implications**

EDRF is the first molecular chaperone of globin proteins to be discovered. Its variable expression may be one explanation for the variable severity of Beta thalassemia seen in patients with identical genotype. Future study of this molecule may lead to development of novel medical therapies for thalassemia and other disorders of hemoglobin synthesis

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