20th International p53 Workshop- Abstract Submission Template

Submission Deadline: January 31st 2026 (5pm EDT)
Notification of acceptance: By or before February 27, 2026

Title of study/project: p53 ser 18 regulates post- prandial glucose homeostasis.

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Year of training:

Abstract:

Purpose
The tumor suppressor p53 integrates stress and metabolic signaling across tissues. While p53 has been implicated in glucose homeostasis, the mechanisms linking p53 signaling to systemic metabolic regulation remain incompletely understood. We investigated whether phosphorylation of p53 at serine 18 (Ser18) regulates postprandial glucose control through adipose tissue metabolic pathways during diet-induced metabolic stress.

Materials and Methods
Wild-type and p53S18A knock-in mice were subjected to high-fat diet (HFD). Glucose tolerance tests (GTT), insulin tolerance tests (ITT), and insulin signaling analyses were performed to assess systemic insulin sensitivity. Adipose tissue transcriptomic profiling was conducted to identify p53-dependent metabolic pathways. Circulating metabolites and hepatic signaling responses were evaluated to determine inter-organ metabolic regulation.

Results
*Under HFD conditions, p53S18A mice exhibited significantly exaggerated glucose excursions during glucose challenge compared with wild-type controls, despite similar systemic insulin resistance as measured by ITT and hepatic AKT signaling. Transcriptomic analysis of adipose tissue revealed marked upregulation of **Folh1**, encoding glutamate carboxypeptidase II, an enzyme involved in folate and one-carbon metabolism. These changes occurred without strong induction of inflammatory cytokines but were accompanied by altered expression of immune surveillance genes. We propose that loss of p53 Ser18 signaling disrupts adipose one-carbon metabolic regulation, altering circulating metabolite pools and hepatic metabolic state. This perturbation delays the suppression of hepatic gluconeogenesis*

following nutrient challenge, resulting in amplified postprandial glucose excursions independent of classical insulin signaling defects.

Conclusions

Our findings identify p53 Ser18 phosphorylation as a key regulatory node linking adipose tissue metabolism to systemic glucose homeostasis. These results suggest that adipose-derived metabolic signals, including one-carbon pathway metabolites, contribute to the regulation of hepatic gluconeogenesis during metabolic stress. This work highlights a previously unrecognized role for p53 in coordinating inter-organ metabolic communication under conditions of chronic nutrient excess.

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