

# Response-based Bayesian Network Approaches for Adaptive Radiotherapy of Non- Small Cell Lung Cancer (NSCLC)

**Yi Luo**, I El Naqa, DL McShan, D Ray, I Lohse, MM  
Matuszak, M Schipper, S Jolly, F-M Kong, RK Ten Haken

*Department of Radiation Oncology,  
The University of Michigan, Ann Arbor, MI, USA*

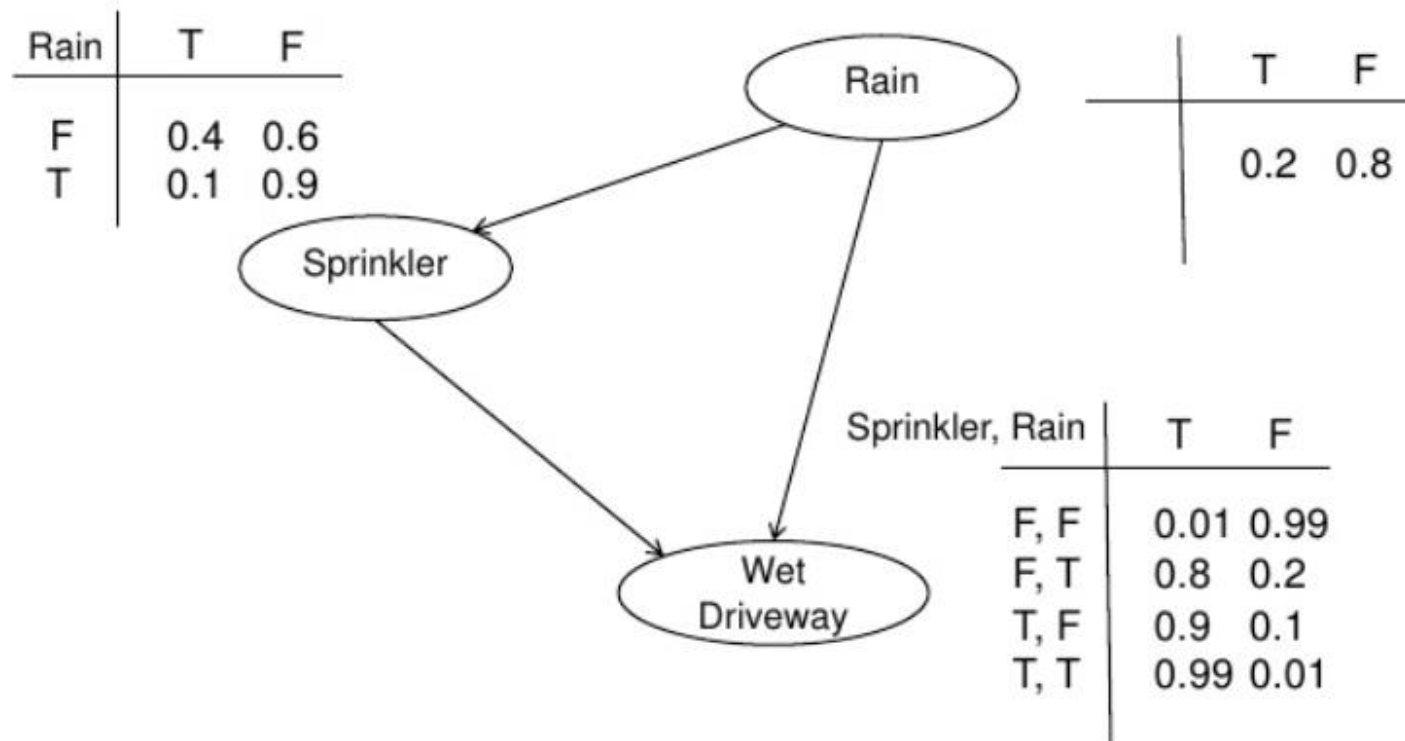
# Purpose

- **Personalized NSCLC radiotherapy intends to deliver an appropriate amount of dose to control the tumor while reducing radiation-induced toxicities (radiation pneumonitis, esophagitis, carditis)**
- **Radiotherapy outcomes are multi-factorial and may depend on: radiation dose and patients' physical, clinical, biological and genomic characteristics before and during the course of radiotherapy**
- **Our goals are to:**
  - **Identify hierarchical radiobiological relationships influencing observed outcomes in NSCLC**
  - **Develop practical Bayesian Networks (BN) for adaptation of radiotherapy in NSCLC**

# Retrospective Data Set

- Our data included 79 NSCLC patients, 15 with radiation pneumonitis  $\geq$ G2 (RP2).
- Besides mean lung dose (MLD), each patient had 179 features:
  - 10 clinical factors (e.g., age, KPS, smoking status, etc.),
  - 60 single-nucleotide polymorphisms (SNPs)
  - 49 microRNAs
  - 30 cytokines *before* treatment course
  - 30 cytokines *during* treatment course

# Bayesian Networks (BNs)



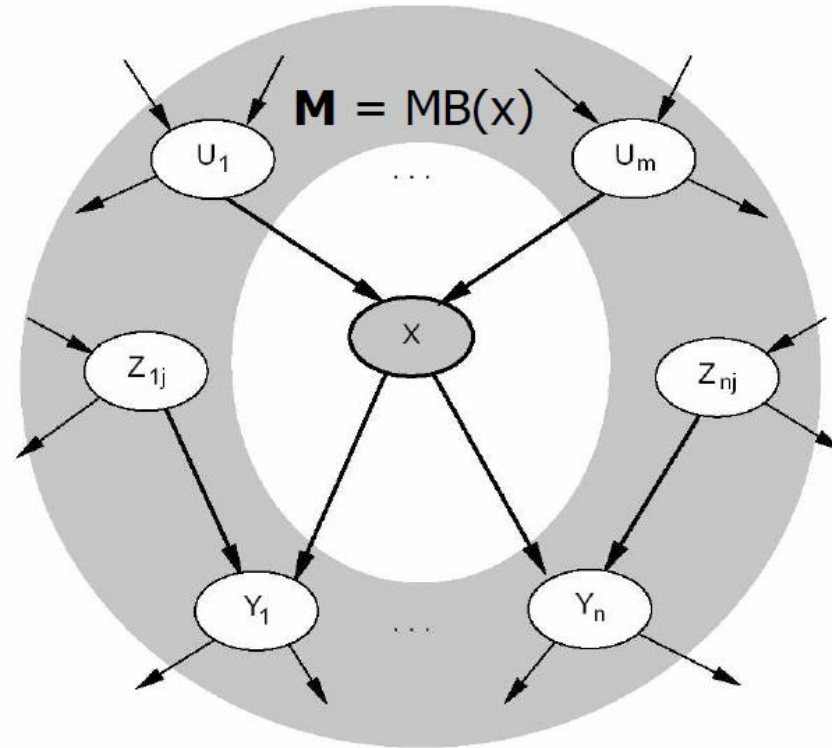
$\Pr(\text{Rain} \mid \text{Wet Driveway})$

$\Pr(\text{Sprinkler Broken} \mid \text{!Wet Driveway} \ \& \ \text{!Rain})$

BNs are belief networks represented by a graph where:

- nodes are variables and
- edges are relationships between variables

# Markov Blanket (MB)

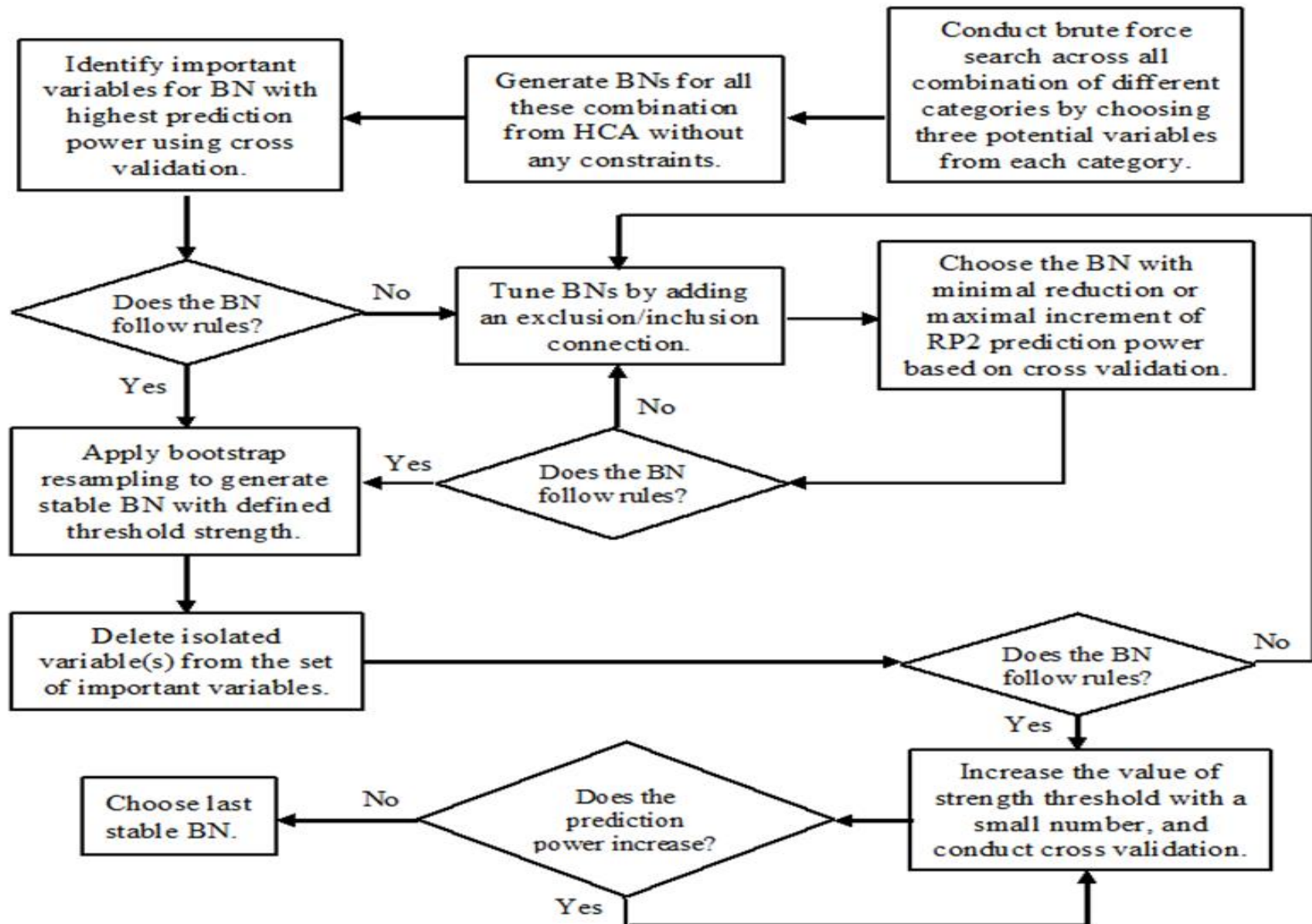


- MB is a feature selection tool for inter-related variables.
- MB of a node is a set consisting of its inner family (parents, children, and spouses)

# Methods

- **A large-scale Markov blanket based on the HITON algorithm was employed for selecting relevant radiobiological predictors of outcomes and extended family of variables.**
- **The corresponding BN structure was obtained by using the Hill-Climbing Algorithm implemented in the R programming environment.**
- **The BN was guarded against overfitting using k-fold cross validation.**

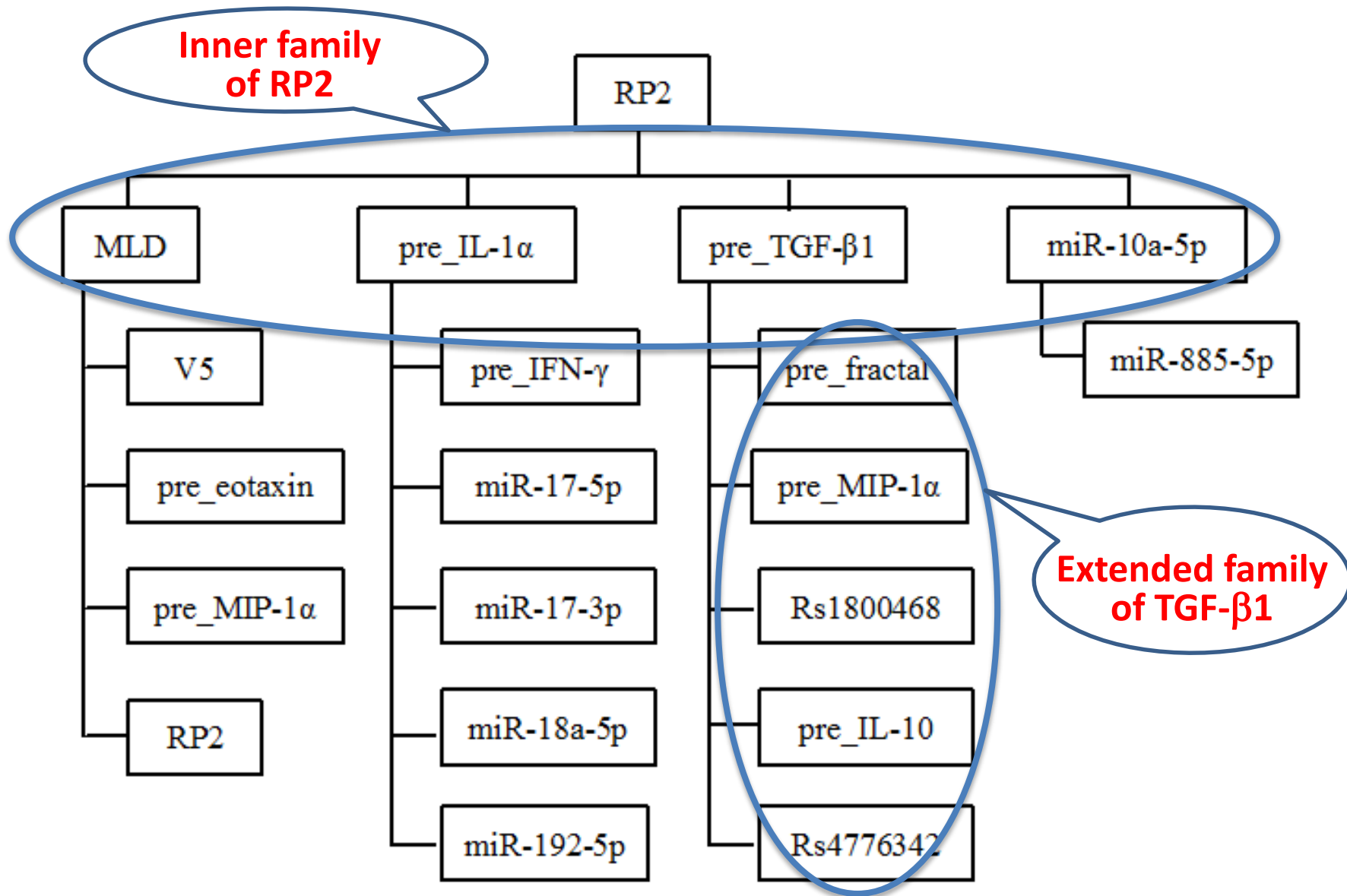
# Overall BN Development Process



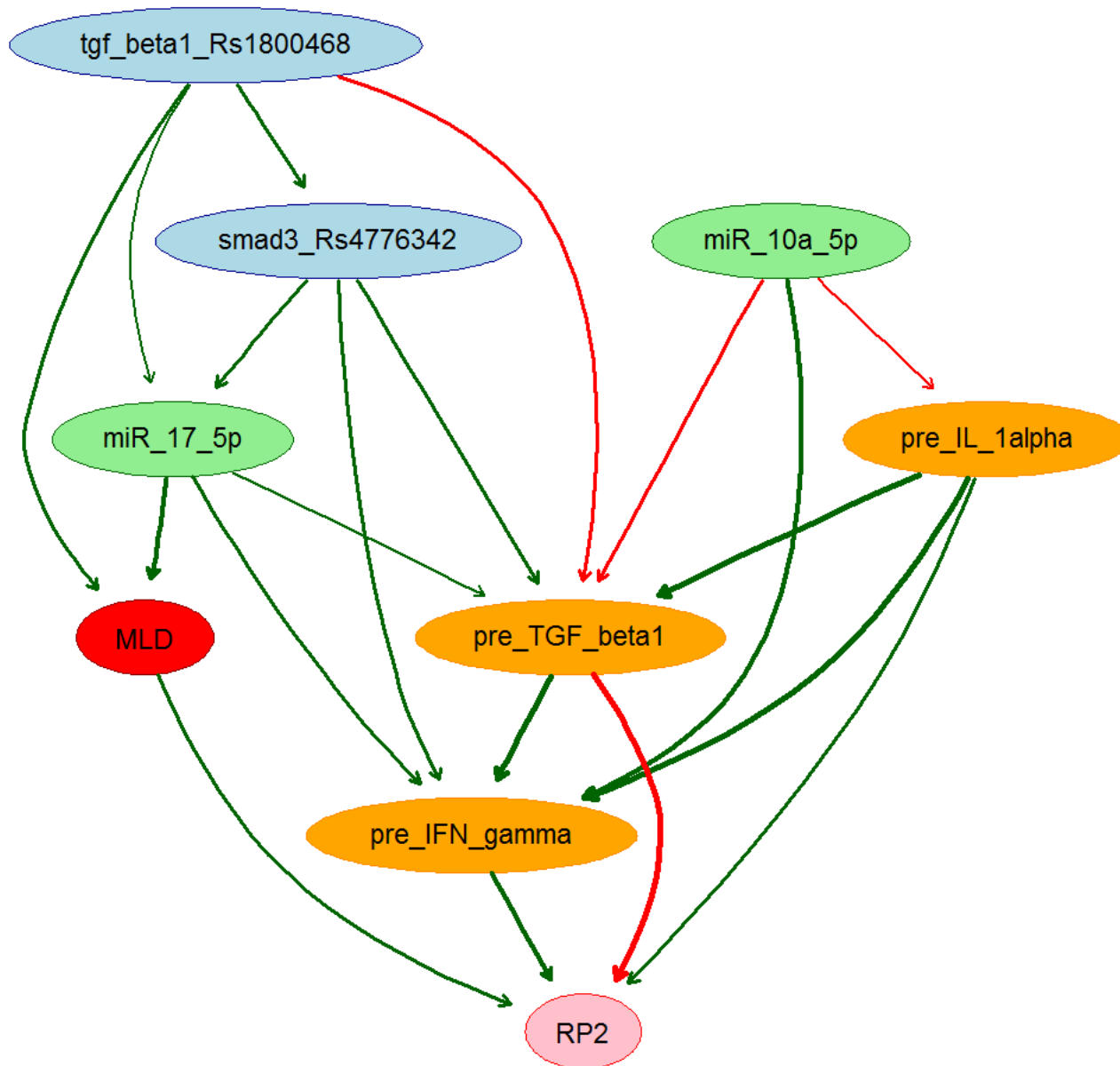
# **Bayesian Networks to Show Hierarchical Biophysical Relationships Influencing RP2**









# Extended MB Neighborhoods of RP2 *before* Radiation Treatment

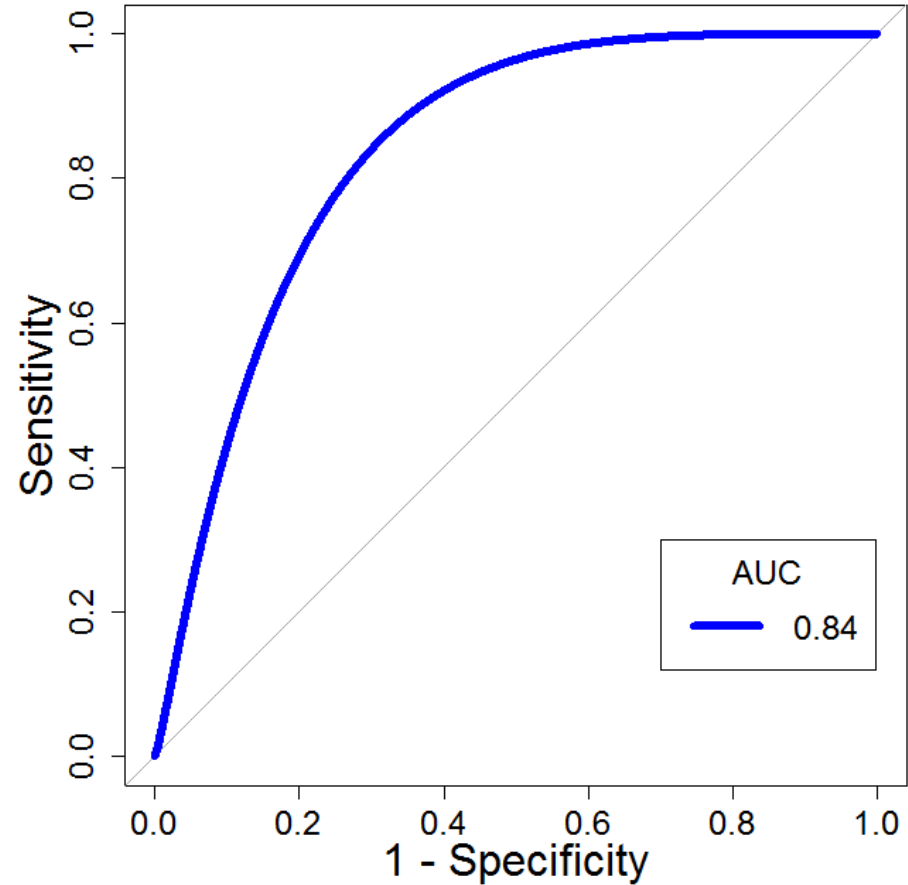
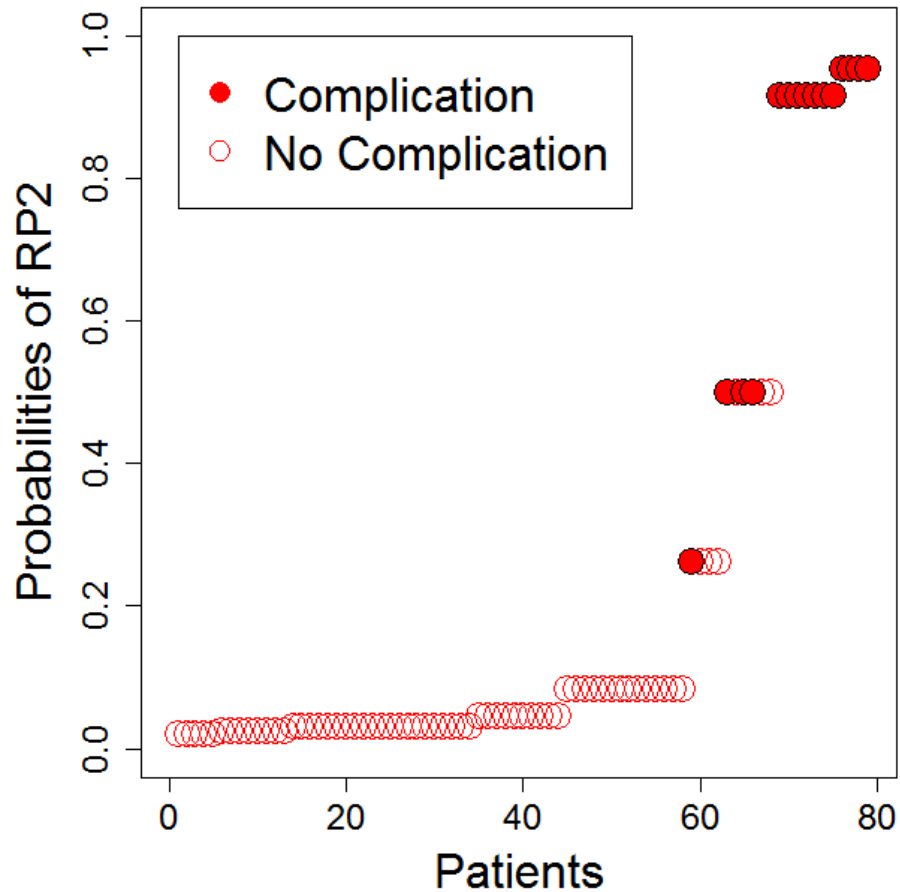


# Pre-Treatment BN for RP2 Prediction

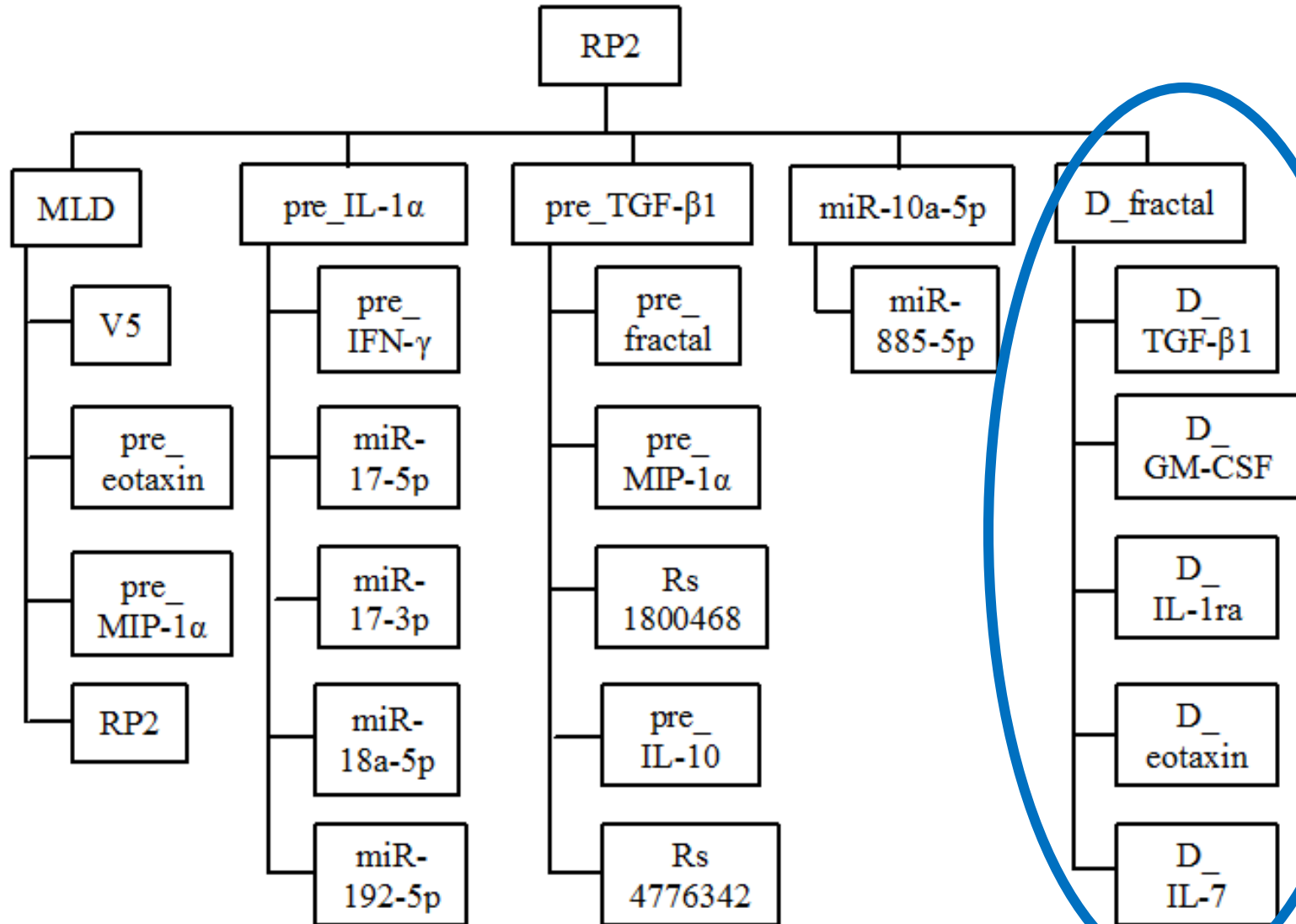


Legend	
	Pretreatment Cytokines
	SNPs
	microRNAs
	Dosimetry
	Positive Influence
	Negative Influence

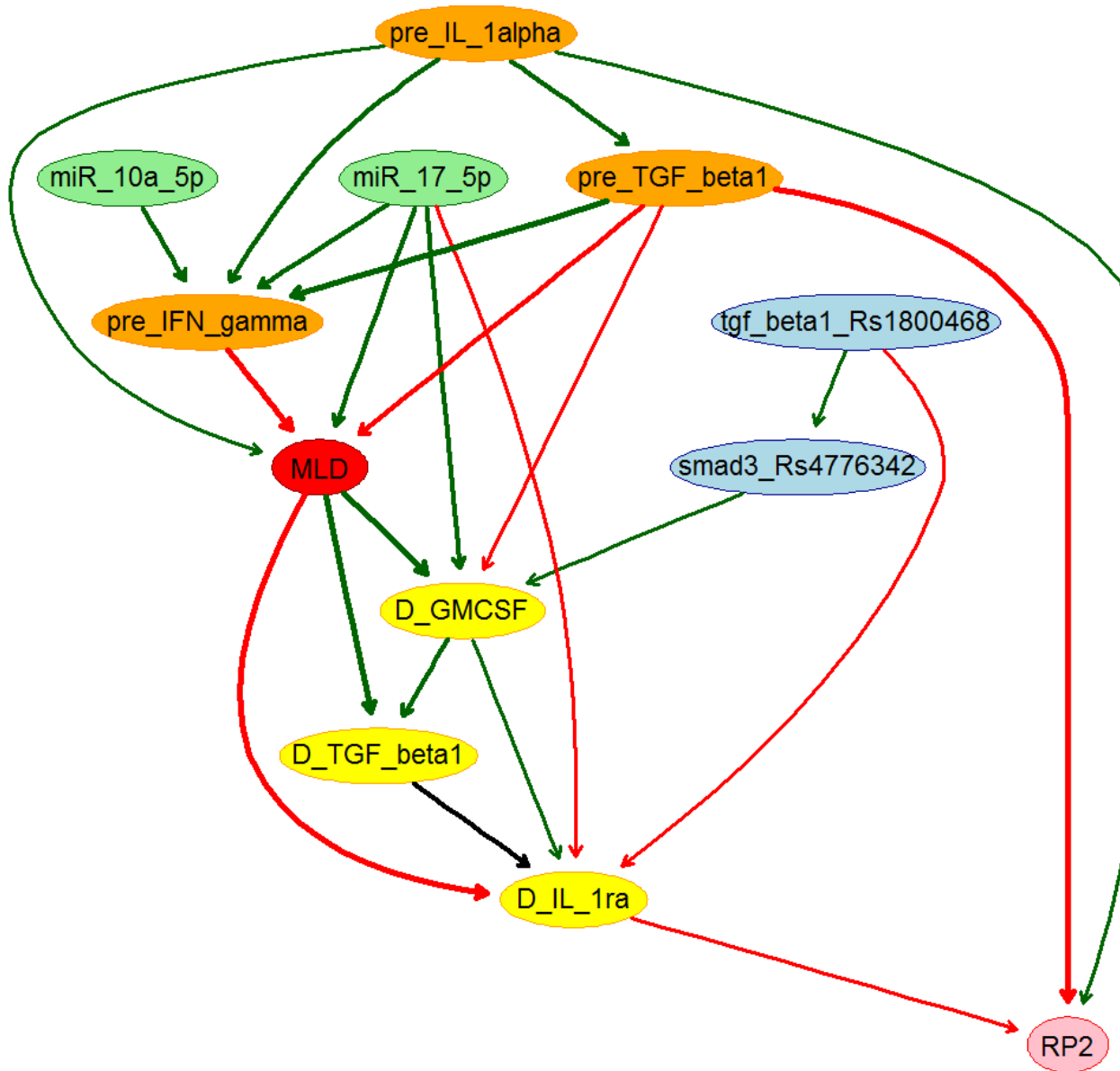
# Evaluation of *Pre-Treatment* BN










# Extended MB Neighborhoods of RP2 *during* Radiation Treatment

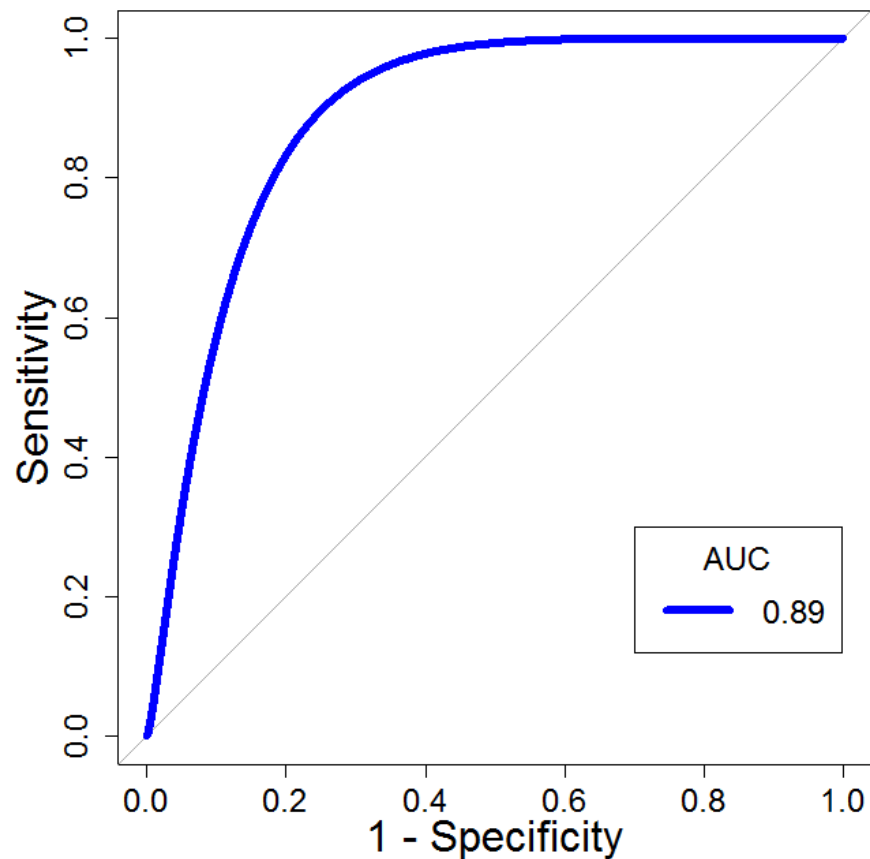
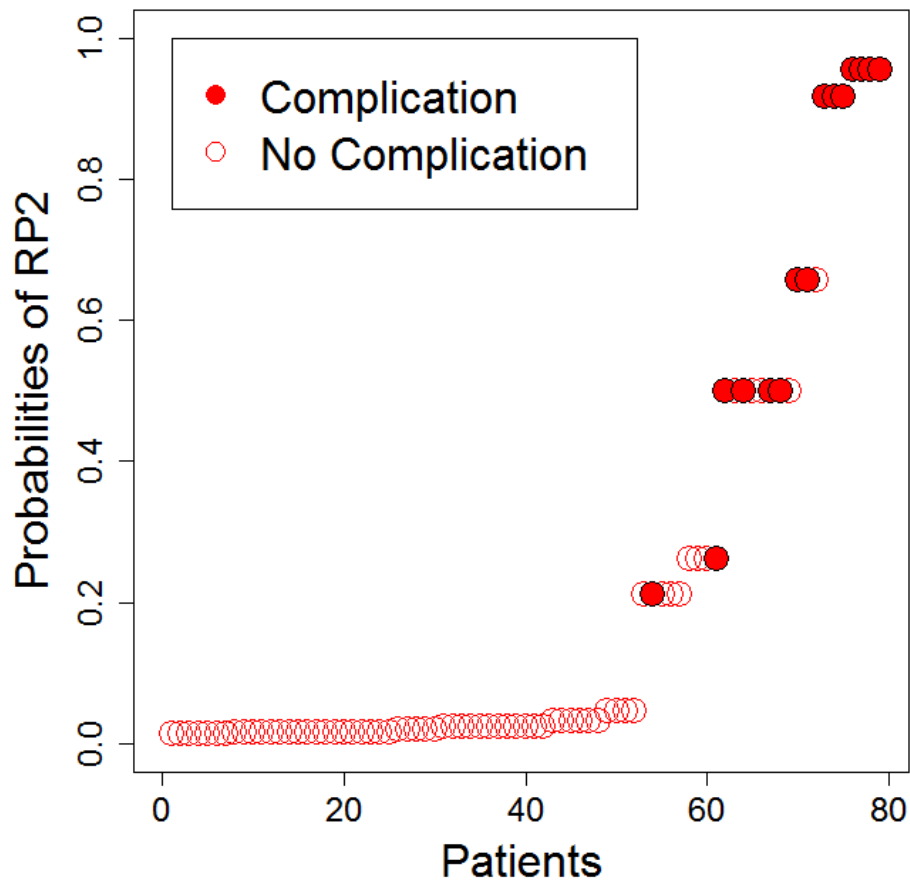


# During-Treatment BN for RP2 Prediction



Legend	
	Pretreatment Cytokines
	During Treatment Cytokines
	SNPs
	microRNAs
	Dosimetry
	Positive Influence
	Negative Influence

# Evaluation of *During-Treatment* BN



# Conclusions

**We developed BN systems to describe the radiation outcomes in NSCLC patients *before and during* the course of radiation treatment based on retrospective data.**

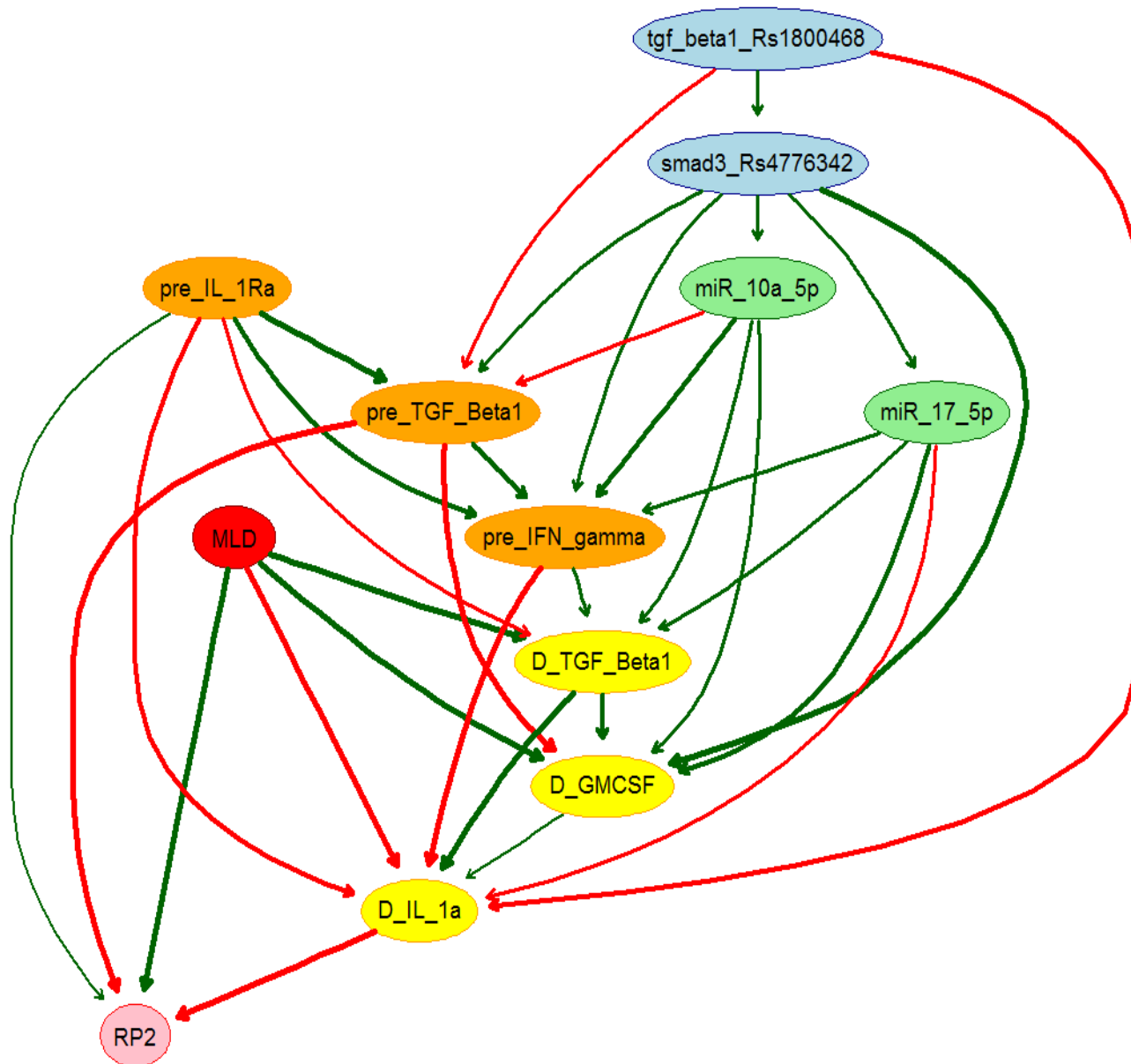
- The prediction performance of the BN improves by incorporating during treatment information.**
- This approach can handle high dimensional predictors and can be an important component of decision support for personalized adaptive radiation treatment.**
- However, it still needs to be validated in external, independent data.**

# Practical BNs

- “Practical BNs” can be *adjusted* from “radiobiological BNs” for *adaptive therapy purposes*, with minor compromise of estimated prediction power.
- Given a patient’s pretreatment data, an appropriate treatment plan can be chosen from a practical BN to control the tumor and keep the radiation toxicities under a certain level.
- When the patient’s during treatment information is available, the planned dose can be adjusted in the BN according to his/her responses, to better control tumor without increasing the chance of the complication.



# A Practical BN for *During-Treatment*



Legend	
	Pretreatment Cytokines
	During Treatment Cytokines
	SNPs
	microRNAs
	Dosimetry
→	Positive Influence
→	Negative Influence